Trajectories of Hyperactivity and Inattention Symptom Scores in Boys of Low Socioeconomic Status: An Assessment of Risk Factors and Cigarette Smoking Behaviors in Late Adolescence and Young Adulthood

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ABSTRACT

Trajectories of Hyperactivity and Inattention Symptom Scores in Boys of Low Socioeconomic Status: An Assessment of Risk Factors and Cigarette Smoking Behaviors in Late Adolescence and Young Adulthood

Wendy Yin Kei Cheng

Attention-deficit hyperactivity disorder (ADHD), once considered a childhood-limited neuropsychiatric condition, is now recognized as often persisting into adolescence and beyond. Recent studies of ADHD and its symptom domains--hyperactivity and inattention--indicate that symptoms can wax and wane over time and follow discrete trajectories characterized by different symptom levels and shapes. However, little is known about symptom trajectories in high-risk groups, such as boys from low socioeconomic backgrounds. Childhood ADHD is associated with cigarette smoking in adolescence, but whether the risk is specific to hyperactivity or inattention or their respective symptom trajectories is not clear.

The aims of my dissertation research were to identify trajectories of hyperactivity and inattention symptom scores in a sample of boys from low socioeconomic backgrounds and to assess the associations of those trajectories with cigarette smoking outcomes in late adolescence and young adulthood.

In pursuit of those aims, I first conducted a narrative literature review to assess current evidence regarding the persistence of childhood ADHD, hyperactivity and inattention into adolescence, and the associations of persistent ADHD and its symptom domains with the risks of cigarette smoking and nicotine abuse and dependence in adolescence and early adulthood. Data on boys of low socioeconomic status, where available, were summarized. Evidence suggests that

nearly 50% of individuals with childhood ADHD or its symptom domains continue to have symptoms in adulthood. Hyperactivity symptom trajectories are likely to decline over time, whereas inattention symptom trajectories are more stable. The sparse literature on the association between ADHD, hyperactivity, and inattention symptom persistence and high symptom score trajectories and smoking outcomes suggests that high inattention symptom score trajectories are associated with earlier onset and higher risk of nicotine abuse or dependence in early adulthood than lower trajectories. Evidence on hyperactivity symptom score trajectories and similar smoking outcomes is inconclusive. Literature on symptom trajectories in low socioeconomic boys is sorely lacking; no study has evaluated the association of symptom score trajectories with smoking outcomes.

Second, in a sample of 1,037 boys from low socioeconomic neighborhoods, I derived trajectories of hyperactivity and inattention symptom scores between childhood and mid-adolescence (ages 6-15 years), using teachers' and mothers' ratings, separately. I also evaluated risk factors for high symptom score trajectories. Three trajectories were identified for both hyperactivity and inattention symptom scores. Hyperactivity symptom scores generally declined over time (high declining, moderate declining, and low declining), whereas inattention symptom scores remained stable (high stable, moderate stable, and low stable). Most boys had low symptom scores over time (i.e., low declining for hyperactivity or low stable for inattention), but approximately one-fifth to one-third followed high symptom score trajectories (high declining for hyperactivity or high stable for inattention). Mothers were more likely than teachers to rate boys as having higher symptom scores. Boys' behavioral symptom scores (hyperactivity, inattention, opposition, and anxiety) at age 6 years and lack of family intactness were risk factors for high hyperactivity and inattention symptom score trajectories.

Third, in the same sample of boys from low socioeconomic neighborhoods, I assessed the associations of the hyperactivity and inattention symptom score trajectories with frequency of cigarette smoking at ages 16-17 years (late adolescence) and daily and heavy (≥1 pack/day) smoking at ages 23 and 28 years (young adulthood). I further conducted mediational analyses to assess the potential impact of cigarette smoking frequency and use of alcohol, marijuana, and other drugs in late adolescence on smoking outcomes in young adulthood. High vs. low symptom score trajectories of hyperactivity (i.e., high declining vs. low declining) and inattention (i.e., high stable vs. low stable) were associated with nearly doubled odds of high cigarette smoking frequency (≥40 times in the past year) in late adolescence (hyperactivity: OR=1.97 [95% CI=1.30-2.98]; inattention: OR=1.87 [1.27-2.76]). High (vs. low) symptom score trajectory of inattention, but not hyperactivity, was further associated with elevated risk for daily cigarette smoking (OR=2.67 [1.53-4.64]) and heavy cigarette smoking (OR=1.95 [1.10-3.45]) in young adulthood. Part of the associations (about 11-23%) was mediated by high cigarette smoking frequency in late adolescence. The mediation roles of other substances were not statistically significant.

Although the socioeconomically disadvantaged boys whose data I analyzed were similar in number of symptom score trajectories and trends (declining for hyperactivity and stable for inattention) to boys in general populations, they were at elevated risk for high scores for both of the symptom domains over time. Childhood behavioral problems as well as lack of family intactness were associated with high symptom score trajectories of both hyperactivity and inattention. High trajectories of both hyperactivity and inattention scores were associated with high risk of cigarette smoking frequency in late adolescence, but inattention appeared to have a longer-term impact on smoking behaviors. Altogether, my research findings suggest that children

with high symptom levels of hyperactivity and/or inattention at an early age, especially those with symptoms that persist over time, might benefit from early interventions to manage and reduce their symptoms and their risk of becoming cigarette smokers.

TABLE OF CONTENTS

LIST OF CHARTS, GRAPHS, ILLUSTRATIONS

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DEDICATION

To my soon-to-be-born daughter, who motivated me to persevere through the long days and nights of this journey and who inspires me to be the best version of me each day.

CHAPTER 1

Introduction

Attention-deficit hyperactivity disorder (ADHD) is a neuropsychiatric condition characterized by two symptom domains--hyperactivity/impulsivity and inattention. Once considered a childhood-limited condition, ADHD is now recognized as often persisting into adolescence and adulthood.[1-5] Most extant literature has defined and assessed the persistence of ADHD in terms of its presence, based on criteria set by the Diagnostic and Statistical Manual of Mental Disorders, at two time points.[1-7] Very few studies have evaluated the persistence of ADHD with reference to its two symptom domains.[8-10]

The past decade has seen increased recognition that the symptoms of ADHD can wax and wane over time, and that the number (and severity) of symptoms is positively associated with the risk for negative outcomes.[8,11-14] With the increased adoption of trajectory analytic methods, such as growth mixed models and latent class growth analysis, recent studies have traced the course of ADHD symptoms and symptom domains over multiple time points to characterize the persistence of ADHD more comprehensively.[12,15] Nevertheless, the current understanding of the symptom courses of hyperactivity and inattention symptoms has largely been based on studies of general, mixed-gender samples.[16-21] The literature on high risk groups, such as boys and children of low socioeconomic status, is limited.

Cigarette smoking is associated with a wide range of diseases and is the leading cause of preventable death.[22] Smoking in adolescence is a particularly critical public health concern because individuals who start smoking in adolescence are more likely than those who start later to transition to daily and heavy smoking and to develop nicotine dependence,[23-26] increasing their risk of morbidity and mortality.[27] Research has indicated that children with ADHD are more likely than those without ADHD to smoke cigarettes in adolescence and to progress from ever smoking to daily smoking in early adulthood.[24,28-32] However, the roles of component symptoms

and symptom domains of ADHD are less clear.[24,30,33-38] Some studies have indicated that inattention, but not hyperactivity, is linked to smoking in adolescence and young adulthood.[39-43]

A few studies of the relationships of trajectories of hyperactivity and inattention symptoms with smoking outcomes in adolescence and early adulthood have found the risk of nicotine abuse or dependence to be twice as high among subjects in high inattention score trajectories as among subjects in lower symptom trajectories.[44,45] Associations of smoking outcomes with hyperactivity symptom trajectories are unclear. Moreover, such outcomes may be too rare during early adolescence or even early adulthood for meaningful evaluation.[42]

My dissertation research aimed to fill the gaps in current literature on trajectories of hyperactivity and inattention symptoms among boys from low socioeconomic backgrounds and the associations of the symptom trajectories with cigarette smoking behaviors in late adolescence and young adulthood.

Chapter 2 is a narrative review of literature on the persistence of childhood ADHD and its symptom domains over time, and on the associations of symptom trajectories with the risks of cigarette smoking and nicotine abuse and dependence in adolescence and early adulthood. In this review, I aimed to identify key findings and gaps in the literature, especially those on boys of low socioeconomic status, to inform the empirical research for my dissertation.

Prior studies have largely operationalized persistence as either (i) the proportion of individuals with ADHD (or its symptom domains) in childhood who continue to have ADHD (or its symptom domains) at follow-up during early or mid-adolescence, or (ii) the trajectory of symptoms over two or more time points. I therefore assessed persistence separately for studies using the proportion approach and the trajectory approach. I further noted considerable differences in design among studies, by study population (i.e., clinically referred vs. community

sample), gender distribution, informant source (i.e., caregiver, teacher, participant, or multiple informants), and assessment method used (i.e., clinical interviews vs. questionnaires). To account for such differences, I stratified the assessment of persistence by the various study design characteristics.

Chapter 3 describes the first of two empirical studies I conducted using data on a sample of boys from low socioeconomic neighborhoods in Montreal, Canada, obtained from the Longitudinal and Experimental Study of Low Socioeconomic Status Boys.[46] In my study, I derived trajectories of hyperactivity and inattention symptoms from scores provided by teachers and mothers, separately, from childhood to mid-adolescence (by teachers at age 6 years; by teachers and mothers annually at ages 10-15 years). I then evaluated potential risk factors for high symptom score trajectories, including parental/familial factors and boys' baseline behavioral symptoms.

By utilizing latent class growth analysis, I constructed the trajectories of the two symptom domains of ADHD from data collected over multiple time points and depicted symptom fluctuations over time. I did so using both teacher and mother ratings separately, so as to home in on the unique perspectives of the two informants.

Most of the few studies of risk factors for symptom developmental courses have focused only on a small set of individual characteristics or parental/familial influences; very few have accounted for both. Studies of parental risk factors have largely evolved around maternal factors; little is known about paternal factors. In Chapter 3, I analyzed a comprehensive list of maternal, paternal, and familial factors as well as a set of boys' externalizing and internalizing behavior symptoms in childhood.

Chapter 4 describes the second empirical study, which uses data on the same sample of boys from low socioeconomic neighborhoods as the previous chapter. In this study, I investigated the associations of trajectories of hyperactivity and inattention symptom scores from childhood to mid-adolescence with cigarette smoking frequency at ages 16-17 years (late adolescence) and daily and heavy (one pack or more per day) cigarette smoking at ages 23 and 28 years (young adulthood). In assessing cigarette smoking outcomes in young adulthood, I distinguished direct effects from indirect effects mediated by cigarette smoking frequency alone and in combination with frequency of alcohol use, marijuana use, and other drug use in late adolescence. This study is one of the first to investigate the associations of trajectories of hyperactivity and inattention symptom scores with smoking outcomes that are age-appropriate for late adolescence and young adulthood. By assessing both hyperactivity and inattention symptom scores, I was able to investigate whether risks of smoking outcomes were unique to either symptom domain. Unlike past studies, which largely focused on the role of smoking initiation or lifetime smoking in adolescence, I analyzed frequency of cigarette smoking in late adolescence as a prognostic factor of daily and heavy cigarette smoking in young adulthood, in order to highlight the role of adolescence as a sensitive developmental period with potentially profound implications for adult life.

Chapter 5 summarizes the findings and conclusions from the previous chapters, describes their public health implications, and suggests future directions. Research on the associations of trajectories of hyperactivity and inattention symptom scores in risk groups with cigarette smoking outcomes is scarce. My dissertation research represents an effort to address these gaps by identifying symptom score trajectories in a sample of boys from low socioeconomic

neighborhoods and assessing the risks they pose for cigarette smoking outcomes that are age-appropriate for individuals in late adolescence and young adulthood.

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CHAPTER 2

Persistence of ADHD and hyperactivity and inattention symptoms between childhood and adolescence, and smoking outcomes in early adulthood: a review and synthesis

ABSTRACT

Background: Although childhood attention deficit hyperactivity disorder (ADHD) and its symptoms can persist into adolescence, little is known about their specific trajectories and outcomes. For example, although children with ADHD are known to be more likely than others to become cigarette smokers, the relationship between year-to-year variations in ADHD symptoms and smoking outcomes is largely unknown.

Objective: This narrative systematic review summarized current literature on the persistence of childhood ADHD and its symptom domains over time, and on the association of symptom trajectories with smoking outcomes.

Method: A systematic search for published reports on the persistence of ADHD or of hyperactivity or inattention symptoms meeting study inclusion criteria and published in English from January 1985 through February 2019 was conducted using PubMed and PsycINFO databases.

Results: Of the 1,464 initial articles generated from our systematic searches, 34 met the inclusion criteria. ADHD was found to persist from childhood into adolescence in more than half of the study participants. ADHD symptoms and hyperactivity symptom score trajectories could be categorized as high, high declining, moderate declining, moderate, low increasing, or low. Inattention scores were found to follow three trajectories—high, moderate, and low. High inattention score trajectories were associated with earlier onset and higher risk of nicotine abuse or dependence in early adulthood than lower trajectories. Evidence on hyperactivity and smoking was inconclusive.

Conclusions: The literature supports the persistence of childhood ADHD and its symptoms into adolescence, the decline of hyperactivity symptom scores over time, the comparative stability of

inattention scores, and the association of high inattention score trajectories with nicotine abuse or dependence in early adulthood. Future studies are warranted to assess more specific smoking outcomes in relation to high symptom trajectories to identify at-risk individuals in need of preventive interventions.

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a childhood-onset neuropsychiatric disorder characterized by inattention and excessive levels of physical activity and impulsivity. Its prevalence is estimated at 7.2% among individuals under the age of 18 years.[1] Once thought of as a condition limited to childhood, it is now well documented that ADHD can persist into adolescence and beyond. Among individuals diagnosed with ADHD in childhood, some studies have reported that two-thirds continue to display the diagnosis in late adolescence.[2-4] The persistence of ADHD has further been shown to differ by its two symptom domains; studies indicate that hyperactivity may dissipate over time, whereas inattention tends to remain stable as individuals age.[5,6] In a recent meta-analysis, among children with the inattentive subtype per the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria, 40% were shown to have the same subtype at the five- to nine-year follow-up in adolescence, whereas among children with the hyperactivity subtype at baseline, 15% had the same subtype at follow-up.[7] However, estimates of persistence of both ADHD and its symptom domains in current literature vary, perhaps due to variations in study design, study populations, definitions of persistence, and informant sources.[5,6,8-13]

Available literature has further indicated that symptoms of ADHD and its symptom domains wax and wane over time, calling into question the stability of ADHD as a condition and the adequacy of the traditional DSM diagnostic criteria.[14] At the same time, the Research Domain Criteria developed by the National Institute of Mental Health (NIMH) indicate that the DSM diagnostic criteria do not integrate adequately with advancing knowledge from genetics and neuroscience.[15] As a result, our understanding of mental illness has gradually shifted from the traditional diagnostic conditions represented in the DSM to a core symptom-based paradigm

comprising a matrix of functional domains that may cut across multiple disorders. Increasingly, ADHD and its symptom domains are recognized not just as diagnostic conditions but also as symptoms that may take different developmental courses over time.

ADHD is associated with several short-term and long-term social, behavioral, and health risks, among which cigarette smoking and nicotine dependence are well studied public health problems.[16-25] Children with ADHD are more likely than other children to smoke cigarettes in adolescence, to smoke daily in early adulthood, and to develop lifetime nicotine abuse and dependence.[22-27] Available evidence has further indicated that childhood inattention rather than hyperactivity is associated with this increased risk of smoking, perhaps reflecting self-medication to improve attention.[28-34] A few studies, however, have found associations of hyperactivity with elevated risk of cigarette smoking, perhaps because of behavioral disinhibition.[35-38]

Most studies of the relationship of ADHD and its symptom domains with cigarette smoking assess ADHD and its symptom domains at one time point, most often in childhood.[22-27] The few studies that assess the course of ADHD and its symptom domains over time generally suggest that among children with ADHD, those who continue to present with ADHD in late adolescence and beyond have higher risks of cigarette smoking and daily smoking than those who do not.[4,39] Such findings call for increased research on the persistence and fluctuations of ADHD symptoms and for the development of interventions in childhood to prevent ADHD symptom persistence.

The objective of this study was to systematically review the literature in order to provide a broader, multi-study estimate of the degree to which childhood ADHD, hyperactivity and inattention persist into adolescence and to assess the associations of various trajectories of ADHD and their symptom domains over time with the risks of cigarette smoking and nicotine

abuse and dependence in adolescence and early adulthood. Because of the known variability of study designs and the expected scarcity of studies on persistence, a meta-analysis was deemed not possible. This study was designed to be a narrative systematic review of existing literature.

METHODS

We identified relevant articles on observational studies published from 1985 through the first week of February 2019 for review using PubMed and PsycINFO databases. Key words used as search terms included the National Library of Medicine Medical Subject Heading terms for attention-deficit disorder with hyperactivity and hyperkinesis, as well as *attention deficit hyperactivity disorder, inattention, inattentive, hyperkinesis, hyperactive, hyperactivity, persistence,* and *trajectories.* No limits were used in either PubMed or PsycINFO searches. Appendix 1, Table 1 presents the search strategy.

We reviewed the titles, abstracts, and full texts of all articles extracted based on the search terms against the following inclusion criteria: 1) the article was published in English; 2) the sample consisted of humans; 3) the study was prospective or retrospective; 4) ADHD, attention-deficit disorder [with or without hyperactivity], ADHD subtypes [i.e., inattentive subtype, hyperactivity-impulsive subtype, combined subtype], or ADHD symptoms [i.e., inattention symptoms, and hyperactivity or impulsivity symptoms]) were assessed as psychiatric conditions of interest, 5) ADHD or its symptom domains were evaluated for persistence, operationalized as (i) the proportion of participants with symptoms of ADHD, hyperactivity, or inattention in childhood (before age 10), who continued to have symptoms at a later time point, such as adolescence (ages 10-17), or (ii) the trajectory of symptoms over two or more time points, where the initial assessment was conducted in childhood, and subsequent assessments were performed in adolescence. Studies were eligible if all participants were younger than 10

years of age at the time of baseline assessment and all were aged 10-17 years at the time of assessment of persistence. Further details on the definition of persistence are provided in the sub-section that follows. Excluded studies were 1) case series, editorials, reviews, treatment trials, abstracts, dissertations, and protocol papers; and 2) case-control studies due to their potential recall bias. We reviewed studies listed in both PubMed and PsycINFO, and eliminated duplicates. Multiple articles reporting the same findings from the same study were evaluated, and only the original article was retained in this literature review. The first author assessed all potential studies for eligibility prior to data extraction. An advisory committee then reviewed the final set of articles to ensure that they all met the inclusion criteria. Data from the final set of articles were extracted and summarized, focusing on sample characteristics, study design, informant source, assessment method used, definition of ADHD and its symptom domains, and findings on persistence. Although the inclusion criteria for articles did not specify outcomes other than persistence, we extracted information on cigarette smoking and nicotine abuse and dependence in adolescence or early adulthood if such data were reported in the articles. Data abstraction followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[40]

Methodological approaches to assessment of persistence

The assessments of persistence were conducted separately for studies using the proportion approach or the trajectory approach. In the proportion approach, we analyzed persistence as the proportion of individuals with ADHD (or its symptom domains) in childhood who continued to have ADHD (or its symptom domains) at follow-up during early or mid-adolescence. In the trajectory approach, we analyzed persistence based on growth curves (i.e., trajectories) reported in the studies using data from multiple time points and statistical methods

including linear latent growth curve modeling, growth mixture modeling, and group-based growth modeling. Such trajectory methodologies synthesize the distribution of all developmental courses of ADHD or symptom domains in the population, and identify discrete growth patterns by organizing similar courses into groups. This approach creates discrete trajectories, each consisting of a group of study participants who have similar developmental courses of ADHD or symptom domains.

In an attempt to provide quantitative summary measures of persistence estimates across studies, where available, we pooled estimates based on studies using the proportion approach or the trajectory approach and summarized them using medians and ranges. For the proportion approach studies, we calculated the median and range of the proportions of individuals who continued to have ADHD or its symptom domains in adolescence. For the trajectory approach studies, we computed the median and range of the number of trajectories and the median proportion of individuals in each trajectory.

Stratified reporting of persistence

To account for differences in design among studies, including study population (i.e., clinically referred vs. community sample), gender distribution, informant source (i.e., caregiver, teacher, participant, or multiple informants), and assessment method used (i.e., clinical interviews vs. questionnaires), we stratified the assessment of persistence by the various characteristics of study design as described, where sufficient sample sizes of comparable studies were available.

RESULTS

A total of 1,464 records were generated from the electronic searches using PubMed and PsycINFO databases. Upon removal of 217 duplicate records, we assessed the titles and, if

available, abstracts of 1,247 articles for eligibility. After elimination of 1,082 ineligible records, we retrieved the full-text articles of 165 records and assessed them for eligibility. A total of 131 articles proved ineligible, leaving 34 articles that met the inclusion criteria and were included in the current literature review. Figure 2.1 is a flow diagram of the search strategy and method of article selection.

Overall study characteristics

Of the 34 studies, 29 were based on community samples and five on clinically referred samples. Nine studies were conducted in the United States, eight in Canada, four in the United Kingdom, and 13 in Australia, Brazil, France, the Netherlands, New Zealand, South Korea, Sweden, Switzerland, or Taiwan. Eighteen studies assessed the persistence of ADHD, and 15 studies assessed its symptom domains as subtypes or symptom levels (four assessed hyperactivity only, one inattention only, and 10 both). No studies assessed the association of the persistence of ADHD and cigarette smoking or nicotine abuse or dependence. Two studies evaluated the persistence of hyperactivity and inattention and the risk of nicotine abuse and dependence.

Persistence of ADHD

Study characteristics

Eighteen studies assessed the persistence of ADHD from childhood to adolescence, with a median follow-up length of eight years and a range of four years to 15 years (Table 2.1a). Of these studies, eight assessed persistence using the proportion approach and 10 studies used the trajectory approach. Most studies that employed the proportion approach categorized children as having ADHD if they met all the DSM-IV criteria. A few studies employed other criteria, including having symptom scores above a cutoff on a hyperactivity/inattention rating scale. In

studies that adopted the trajectory approach, the diagnosis of ADHD was based on a symptom score on a rating scale, such as the Child Behavior Checklist (CBCL), the Diagnostic Interview Schedule for Children (DISC), the Strengths and Difficulties Questionnaire (SDQ), the Social Behavior Questionnaire (SBQ), or the Caretaker Child Symptom Inventory (CSI-4).

Persistence of ADHD based on the proportion approach

Table 2.2a summarizes results generated from studies based on the proportion approach. About half the children (median 50.8%, range 43.8%-75.5%) participating in the eight studies that evaluated the persistence of ADHD by proportion continued to exhibit ADHD during adolescence.[8-12,41-43] The proportion with persistent ADHD was higher (median 61.8%, range 46.4%-66.7%) in the three studies of clinically referred children[11,12,42] than in the five studies of community-based samples (median 49.6%, range 43.8%-75.5%).[8-10,41,43]

Because all studies utilized mixed-gender samples and none stratified by gender, the potential effect of gender on the persistence of ADHD could not be assessed.

Studies varied in type of informant; most studies utilized caregiver reports alone, but some used either caregiver reports paired with teacher reports or caregiver reports paired with participant self- reports, marking ADHD as present if at least one informant marked it as present. Type of informant was not associated with the proportion considered to have persistent ADHD. For instance, across studies that utilized community samples, those based on caregiver reports alone (n=3)[8,10,41] found a median of 49.6% (range: 43.8%-75.5%) of individuals with ADHD persistence compared to 52.0% and 49.2% in studies based on caregiver plus teacher reports (n=1)[43] and caregiver plus participants reports (n=1),[9] respectively.

The number of studies that utilized interviews versus questionnaires to collect ADHD data was similar, and those based on questionnaires yielded a slightly higher proportion of individuals with persistence.[8-10,41,43]

Persistence of ADHD based on the trajectory approach

Table 2.2b summarizes results generated from studies based on the trajectory approach. The 10 studies of trajectories of ADHD over time found a median of 3.5 (range 2-5) trajectories, typically one chronically high symptom level trajectory, one chronically moderate symptom level trajectory, one moderate but declining (also known as childhood-limited) symptom level trajectory, and a chronically low symptom level trajectory.[44-53] Across studies reporting four trajectories (n=4), the majority of individuals (median: 71.8%; range: 5.7%-82.8%) exhibited the chronically low symptom level trajectory, whereas a small proportion of individuals comprised the chronically high symptom level trajectory (median: 13.0%; range: 3.9%-21.6%).[48,50,51,53] The remaining individuals were split between the chronically moderate symptom level trajectory (median: 7.7%; range: 4.7%-47.3%) and the moderate declining symptom level trajectory (median: 10.9%; range: 1.2%-32.0%).

All studies of ADHD trajectories were based on community samples.

Nine studies used mixed-gender samples but one used an all-male sample.[50] About 20% of its participants, who were from low income families, followed a high trajectory, but only a median of 3.9% of the participants in mixed-gender studies did so (n=3). In another study, by Forbes and colleagues, based on a mixed-gender community sample, five trajectories were identified--very high increasing, high increasing, mild, low, and very low. While only a small proportion of the overall sample exhibited the very high increasing trajectory (3.7%), 81.3% were males; 27.6% of participants followed the very low trajectory, and 35.9% were male.

Seven of the ten studies relied on caregiver reports alone,[44,46-49,51,53]; two studies relied on teacher reports alone (n=2)[45,52], and one on a combination of caregiver and teacher reports (symptoms endorsed by either informant).[50] Because of the heterogeneity in other design aspects of these studies, it was not feasible to assess the effect of informant type on results.

More than half of the studies (n=7) were based on caregiver or teacher self-administered questionnaires,[44,45,48,50-53] but because of the heterogeneity in the study design across these studies and in studies that utilized structured interviews (n=3) for data collection, comparisons were not possible to assess the potential impact of assessment method.[46,47,49]

Persistence of hyperactivity

Study characteristics

Fifteen studies assessed the persistence of hyperactivity symptoms; their median length of follow-up was 7 years (range 1-16 years) (Table 2.1b). One study examined persistence based on the proportion approach, and 14 studies used the trajectory approach. Hyperactivity was defined as behavioral or emotional difficulties, and/or treatment intervention for them. In the 14 studies that used the trajectory approach, hyperactivity was assessed as an integer symptom score on a rating scale based on the Aberrant Behavior Checklist, the Basic Personality Index (BPI), the DuPaul's ADHD Rating Scale (ARS), the Swanson, Nolan, and Pelham Rating Scale-IV (SNAP-IV), or the SBQ, and study-specific questionnaires.

Persistence of hyperactivity based on the proportion approach

The persistence study based on the proportion approach was conducted by Lambert and colleagues in the 1980s and evaluated a community sample of boys medically identified as having hyperactivity according to DSM-II criteria at a mean age of 7.7 years.[13] At a mean age of

14.3 years, 43% of the boys were reported by their caregivers as having persistent learning, behavior or emotional difficulties, and as still being treated for hyperactivity (Table 2.2a).

Persistence of hyperactivity based on the trajectory approach

The 14 studies that assessed the trajectories of hyperactivity symptoms over time, described a median of 4 (range: 2-6) trajectories, which typically included a chronically high symptom score trajectory, a high but declining trajectory, a low but increasing trajectory, and a chronically low trajectory (Table 2.2b).[54-67] Most participants were found to exhibit low hyperactivity scores over time; some typically exhibited declining levels of hyperactivity. For instance, in the study by Murray and colleagues and the study by Pingault and colleagues, 59.4% and 74.0% of children recruited from schools in Zurich, Switzerland and Quebec, Canada, respectively, had chronically low symptom scores between childhood and early to mid-adolescence.[60,65] Only 8.0% and 10.3% of the children had chronically high symptom trajectories; 13.0% and16.0% had high symptom scores that declined over time; the remaining 5.0% and 14.3% had low scores that rose slightly over time. However, in the study by Nagin and colleagues, only 20% of boys from low socioeconomic areas in Quebec, Canada, were found to have chronically low symptom scores; 6.0% followed a chronically high symptom trajectory, and 30.0% had high but declining symptom scores over time.[63] The remaining 45.0% followed a unique trajectory of moderate but declining symptom scores as they grew up.

Most studies were based on community samples (n=12),[55,56,58-67], but two were based on clinically referred samples.[54,57] Because the studies also differed in design and number of trajectories, the potential differences in results due to type of sample could not be assessed.

Most studies utilized mixed-gender samples, but a study by Côté and colleagues stratified results by gender, and the studies by Fontaine and colleagues, and Nagin and colleagues

employed 100% female and 100% male samples, respectively.[55,56,63] Findings from such studies suggest that gender may influence hyperactivity trajectories; males were more likely than females to present with consistently high levels of hyperactivity across time. Côté and colleagues, for instance, reported that 36.5% of male participants from a community sample exhibited chronically high levels of hyperactivity and another 35.8% displayed high but declining symptom levels across time. Only 17.8% of female participants, exhibited chronically high levels of hyperactivity and 25.3% had high but declining symptoms.[55] Similarly, in the Fontaine study, which followed a community sample of girls over six years, 19.0% had high levels of hyperactivity that declined with time.[56] In contrast, in the Nagin study, 6.0% and 30.0%, respectively, of male participants (who were from low socioeconomic areas) experienced chronically high or initially high levels of hyperactivity that declined over time.[63]

Most studies of hyperactivity trajectory used either caregiver or teacher informants (n=11).[54-56,58-63,65,66] Two studies used reports from both caregivers and teachers,[57,64] and one used caregivers, teachers, and participants.[67] Compared to caregivers, teachers appeared less likely to report hyperactivity symptoms as elevated, although when they did, they tended to score them as high rather than moderate. For instance, in the study by Murray and colleagues, teachers in schools in Zurich, Switzerland, gave chronically low symptom scores to 63.0% of males and 81.0% of females through mid-adolescence, while caregivers in the study by Tsai and colleagues gave chronically low scores to 52.5% of children recruited from schools in Taiwan.[60,66] However, teachers in the Murray study gave chronically high hyperactivity scores to 24.0% of males and 9.0% of females, while caregivers in the Tsai study gave chronically high hyperactivity scores over time to 6.9% of the children they followed.

Persistence of inattention

Study characteristics

Eleven studies assessed the persistence of inattention symptoms with a median follow-up of 6 years (range 1-16 years) (Table 2.1c).[57-60,62,64-69] All studies utilized the trajectory approach, and found inattention to follow a median of 3 (range: 2-6) trajectories (Table 2.2b). Such trajectories typically were stable; they included a group with chronically high symptom scores, a group with chronically moderate scores, and a group with chronically low scores. Most participants in studies based on general populations were scored low (median: 51.0%; range: 29.0%-65.3%); only a small proportion were scored high over time (median: 12.5%; range: 12.4%-18.8%). Studies of special populations scored larger proportions as high in inattention. For example, the study by Pingault and colleagues, which evaluated predictors of substance abuse or dependence in early adulthood in Quebec, Canada, found four group trajectories for inattention and gave 25.7% of participants chronically high symptom scores.[64]

Ten studies [58-60,62,64-69] were based on community samples; only one by Howard and colleagues was clinically-referred.[57] However, because they differed in study design and the number of trajectories, the potential differences due to type of sample could not be assessed.

All the studies utilized mixed-gender samples, but the study by Larsson and colleagues in Sweden reported gender distribution within the two trajectories of inattention symptom identified,[58] and the study by Murray and colleagues in Switzerland separately analyzed symptom trajectories by gender.[68] Both studies utilized community samples and found that larger proportions of males were scored in the high symptom trajectory. In the Larsson study, of the 14% of the sample who exhibited a high/increasing trajectory, 62.0% were males. Likewise, in the Murray study, 39.0% of males but no females exhibited chronically high symptom scores, while 10.0% of females but no males exhibited high but declining symptom scores.

Five studies were based on teacher reports only [60,62,65,68,69], and three on caregiver reports only [58,59,66]; two used combined reports by caregivers and teachers[57,64] and one used reports by caregivers, teachers, and participants.[67] Studies based on caregiver versus teacher reports yielded similar results in terms of distributions of individuals into high, moderate, or low symptom level trajectories. Teachers' scores were more likely than caregivers' scores to follow a high but declining symptom trajectory, but only in a small proportion of individuals. For instance, in the study by Robbers and colleagues, approximately 14.0%-21.0% of the male and 20.0% of the female participants presented with high declining symptom trajectories, unlike other caregiver-based studies.[69]

Because all studies were based on questionnaires, the potential impact of assessment method on results could not be evaluated.

Association between ADHD, hyperactivity, and inattention persistence and subsequent cigarette smoking and nicotine use disorder

No study evaluated the association of ADHD persistence with subsequent cigarette smoking or nicotine abuse or dependence in early adulthood.

Two studies, both based on the trajectory approach, assessed the association of ADHD, hyperactivity, and inattention persistence with subsequent nicotine abuse or dependence in early adulthood (mean age: 20.9-21.2), but neither assessed cigarette smoking as an outcome.[56,64] Both studies evaluated participants' nicotine abuse or dependence based on structured interviews using the Diagnostic Interview Schedule. Using a mixed-gender community sample of children from public schools in Quebec, Canada, the Pingault study found that only inattention trajectories and not hyperactivity symptom trajectories were associated with differential risk of nicotine abuse or dependence in early adulthood.[64] Specifically, the three trajectories identified

for hyperactivity between ages 6 and 12--low (endorsed by both teachers and caregivers), high (endorsed by caregivers only), and high (endorsed by both teachers and caregivers) did not differ in risk of nicotine abuse or dependence at a mean age of 21.2 years. However, the high inattention trajectory group had 2.25 times higher odds of nicotine abuse or dependence than the low trajectory group (p-value<0.001), and were also more likely to experience the first symptoms of nicotine use at a younger age. In the Fontaine study conducted on an all-female sample, a high hyperactivity score trajectory was associated with higher odds of nicotine abuse or dependence in early adulthood than the moderate and low symptom trajectories.[56]

DISCUSSION

This review synthesized current literature on the persistence of ADHD and its symptom domains between childhood and adolescence, and its impact on the risk of nicotine abuse or dependence in early adulthood. By adopting a trajectory approach in addition to a proportion approach to assess persistence, this review allowed for a comprehensive view of the developmental course of ADHD and its symptom domains beyond their diagnostic criteria. Among children with ADHD, approximately half in community samples, and nearly two-thirds in clinically referred samples continued to do so in adolescence. Trajectory analyses demonstrated various levels and types of symptom courses. Specifically, overall ADHD symptom scores followed four trajectories—high, moderate, moderate declining, and low. Although most study participants had chronically low symptom scores throughout childhood and adolescence, about 13% had with chronically high symptom scores. Hyperactivity persisted in about 43% of individuals. Its symptom scores followed four trajectories--high, high declining, low increasing, and low. Although most study participants had chronically low symptom scores, and a small proportion exhibited chronically high scores, 13.0% to 16.0% had high symptom

levels during childhood but lower scores as they grew into adolescence. Inattention scores followed three mostly stable trajectories over time and--high, moderate, low. Children in the chronically high inattention trajectory had an earlier onset and higher risk of nicotine abuse or dependence in early adulthood than those in the lower trajectories. Evidence on hyperactivity was inconclusive. Data are lacking on the association between both hyperactivity and inattention symptom trajectories and cigarette smoking outcomes.

Estimates of the persistence of ADHD and its symptom domains computed in this literature review are largely consistent with previous reports.[2-4] Although these pooled estimates contribute to the precision of estimates of persistence of ADHD and its symptom domains in available literature, they do not shed light on the developmental courses of ADHD and its symptom domains. The trajectory analyses in this literature review do so. Notably, ADHD and its symptom domains were found to follow multiple trajectories, differentiated by symptom scores and, for ADHD and hyperactivity, their shapes. Although most study participants had low trajectories of both ADHD and its symptom domains scores, at least one-fourth of them had higher trajectories. These findings suggest that ADHD and its symptom domains are not binary or permanent, as diagnostic criteria may suggest. Rather, many individuals may experience some symptoms of ADHD, hyperactivity, or inattention at some point in their early years.

Moreover, while some individuals had high hyperactivity symptom scores, up to 16.0% of them experienced a decline in scores over time, whereas inattention symptom scores tended to remain stable. This distinction is consistent with the current understanding of the two symptom domains, and may be partly attributable to developmental changes.[70] As children grow up, their symptoms may change, such that using the same symptom checklist or criteria to diagnose individuals with either hyperactivity or inattention may not be developmentally appropriate. For

instance, adolescents are less likely than children to be overtly hyperactive because their brain development enables them to adapt to societal norms and suppress their impulsiveness. As a result, they may no longer meet the criteria for hyperactivity. However, as children go through school, tasks and expectations become increasingly complex and demand more sustained attention. Consequently, attention deficit may become more conspicuous.

In this literature review, gender, informant source, and sampling frame (clinic or community) were shown to be associated with persistence. In particular, males were more likely than females to continue meeting diagnostic criteria in adolescence and to receive high symptom scores for ADHD, hyperactivity, and inattention over time. Although the association of ADHD with male gender has been previously documented, the relationship between gender and the persistence of ADHD is less well known.[71] Males are thought to have higher levels of genetic liability than females. According to the polygenic multiple threshold model, for instance, females have a higher threshold of genetic liability than males to manifest ADHD.[72] Furthermore, males are more likely to act out, thereby exhibiting an increased and persistent risk for hyperactivity over time, whereas females are generally more likely to complain about inattention symptoms. Yet those males who do report inattention may have more severe and more persistent deficits than are reported by females. Notably, among the few studies based on all-male samples as discussed, participants were from low socioeconomic areas. Given that low socioeconomic status is a known risk factor for hyperactivity and inattention symptoms in children, it is possible that the impact of male gender on persistence may be partially modified by low socioeconomic status--a possibility that cannot be tested in the current literature review.[73]

Although based on few data points, the observed higher persistence estimates for ADHD and its symptom domains derived from clinically referred than community-based samples are

likely due to the two samples' inherently different risk profiles. Children with ADHD who are referred to clinics have more noticeable and disruptive symptoms of ADHD and are generally more impaired than children in the community. They may also have more comorbidities, which are linked to worse psychiatric health and put them at a higher risk of developing and maintaining ADHD.[74] Clinically referred individuals also generally receive more clinical care than community individuals due to their underlying psychiatric conditions. As a result, ADHD may appear more persistent because it is more likely to be detected.

The difference in findings on the persistence of hyperactivity and inattention based on different informant sources was slight but worth noting. Compared to caregivers, teachers are generally more likely to report high levels of hyperactivity symptoms and to notice declining trends in inattention symptom levels. Such differences may reflect a combination of rating biases, raters' unique perspectives, and situational variability of ADHD symptoms.[75-79] Because scoring and behavior may be situational and may vary by type of informant, the assessment of ADHD persistence and its trajectories should take into account the perspectives of different informants.

Studies on the association between the persistence of ADHD and its symptom domains and cigarette smoking and nicotine abuse or dependence in adolescence and early adulthood are sorely lacking. Of the two studies identified in this literature review, both assessed nicotine abuse or dependence in early adulthood as the outcome and found high inattention score trajectories to be associated with a doubled risk and earlier onset of nicotine abuse or dependence compared to lower symptom trajectories. The association of hyperactivity symptom trajectories with that outcome is unclear; the Fontaine study suggested increased risk whereas the Pingault study had null findings.[56,64] However, the Fontaine study was based on a 100% female sample and the

Pingault study utilized a mixed-gender sample. Nevertheless, the current findings are consistent with the body of literature on the associations of ADHD with substance use outcomes.[80,81] The development of substance use and substance use-related impairment in adolescents has been attributed by some authors to the behavioral disinhibition component of ADHD,[38] or to self-medication to improve cognitive performance and attention.[82]

Although the two studies suggest a relationship between symptom trajectories and nicotine abuse or dependence, the topic has received very little attention, and unknowns remain:

a) The two studies evaluated smoking outcomes only in early adulthood. Smoking behaviors in adolescence were not evaluated, although adolescence is a sensitive period during which exposure to cigarette smoking is known to increase the risk of continual smoking and progression to more problematic smoking behaviors, including nicotine abuse or dependence, in adulthood.[22,83-85] Understanding smoking behaviors in adolescence is important for evaluating prevalence and for public health interventions.

b) Nicotine abuse or dependence may be too rare during early adolescence or even early adulthood for meaningful evaluation because its prevalence may not have peaked and emerging problems may only be starting at such early ages.[4] In other words, nicotine abuse or dependence may not be an age-appropriate smoking outcome during adolescence and early adulthood, which often are periods when individuals initiate or continue to experiment with smoking. Outcomes that quantify the frequency and amount of smoking may be more informative for this age population, especially because they are prognostic factors of subsequent nicotine dependence later in life.[4]

Findings from this literature review should be interpreted in light of a few limitations:

1. Although we included and evaluated 34 studies in this review, their sample sizes became small upon stratification by symptom domains, and other factors of interest. Given the heterogeneity across studies, however, it was necessary to group studies that were similar in design, study sample, length of follow-up, age at follow-up, etc. when synthesizing data. This effort enabled results to be pooled and analyzed. Nonetheless, because we could not control for those factors, we could not conduct a meta-regression. The conclusions reported here may therefore be biased.
2. The studies of the trajectories of ADHD employed various statistical methods. Specifically, most studies used growth mixture modeling, although some used latent class growth analysis, K-means clustering, and semi-parametric mixture models. All such methodologies had different underlying assumptions regarding the amount of variance allowed within and across different trajectories, as well as the underlying distribution of ADHD symptoms. As a result, these different methodologies may have led to varying conclusions regarding the number and shape of the trajectories observed.
3. Only two studies assessed the association between trajectories of hyperactivity and inattention and subsequent smoking outcomes, making generalizability of these findings difficult. Furthermore, the analyses conducted in these studies did not consistently control for potential confounding factors, such as conduct problems and oppositional behavior problems. Previous studies have suggested that the association between ADHD and substance use may be partially, if not fully, accounted for by such behavioral issues.[28] Hence, the amount of bias intrinsic in the current findings is unknown.

4. As discussed earlier in this Discussion section, outcomes assessed in the two smoking outcome studies were restricted to nicotine abuse or dependence and age of onset of nicotine abuse or dependence. These outcomes were assessed only in early adulthood, perhaps too early in the life course for nicotine abuse or dependence to have developed. Outcomes such as frequency and amount of smoking, which are critical prognostic factors for nicotine abuse or dependence in life, might have been more age-appropriate.
5. This literature review included only peer-reviewed articles listed in PubMed and PsycINFO. Gray literature presented in conferences and published elsewhere, such as guidelines, government publications, etc. was not evaluated. If findings were considerably different in such literature, conclusions in the current review may be biased. Additionally, because studies with positive results were more likely to be published than studies with null findings, our findings may have been influenced by publication bias.
6. This literature review included only studies published in English. If studies published in other languages were systematically different from English studies (e.g., different participant demographics or cultures), the current literature review may have been affected by selection bias, and generalizability of the current results may be limited.

Despite these limitations, this review provides an overview of the current understanding of the persistence of ADHD and its symptom domains, from both a conventional diagnostic perspective and a trajectory perspective looking at symptom courses over time. The current findings indicate that ADHD and its symptom domains persist, and that hyperactivity symptoms may decline over time, while inattention symptoms may stay relatively stable. The review also

found that subgroups of children may follow different trajectories; males and clinically referred individuals may be more likely than females and children in the general population to receive high symptoms scores over time. External factors that might affect estimates of persistence include informant type, given that caregivers and teachers may have different perspectives on symptoms.

The limited available data suggest that individuals with high symptom scores for hyperactivity or inattention over time may be at high risk for nicotine abuse or dependence. Additional studies of such associations are needed and should take into account the potential effects of gender (especially in the context of low socioeconomic status), and informant source as well as other potential confounding and mediating factors. The results of such studies could help clinicians detect problematic development patterns among children with high symptoms of ADHD, hyperactivity and inattention early on, and implement timely educational or therapeutic interventions to prevent persistence and subsequent smoking behaviors.

Table 2.1a. Studies reporting the persistence of attention-deficit hyperactivity disorder (ADHD) symptoms and subsequent smoking outcomes

Reference	Sample type	Study design	Main informant source	Assessment strategy	Definition of ADHD	Description of persistence	Smoking outcomes
Proportion approach							
Community sample							
Lecendreux 2015 [8]	**Community sample (N= 875)** - Participants from random digit dialing in France **About 50% male**	**Prospective cohort study** - 4-year follow-up **2 assessments** - Baseline (ages 6-12) and 4 years later (ages 10-16)	Caregiver	Interview using KSADS-C	Meeting full or subthreshold DSM-IV criteria (3 symptoms of either and/or hyperactivity symptoms)	**Full threshold persistence:** 43.8% **Subthreshold persistence:** 22%	-
Liu 2018 [41]	**Community sample (N= 10,090)** - Participants from two parallel cohorts (birth and kindergarten cohorts) from the Longitudinal Study of Australian Children (LSAC) **51% male**	**Prospective cohort study** - 10-year follow-up **6 assessments** - (Birth cohort) Baseline (mean age: 0-1) and biannually to ages 10-11; (Kindergarten cohort) Baseline (mean age: 4-5) and biannually to ages 14-15	Caregiver	Interview using a study-specific questionnaire	Yes to a question regarding presence of ADHD	49.6%	-
McAuley 2017 [9]	**Community sample (N= 130)** - Participants from outpatient clinic for youth with attention, learning, and/or behavioral	**Prospective cohort study** - 5-year follow-up **2 assessments** - Baseline (mean age: 8.9)	Caregiver and participant (endorsed by either of the two)	Interview using KSADS-PL and CGAS for impairment	Meeting full DSM-IV diagnostic criteria, or threshold symptoms but remitted impairment,	Remittent: 18.5% Remitted impairment: 16.9% Remitted symptoms: 15.4% Persistent: 49.2%	-

	difficulties in Canada **75% male**	and follow-up (mean age: 14)			or remitted symptoms but continued to be impaired, or fully remitted		
Parkes 2014 [10]	**Community sample (N= 4,798)** - Participants from birth cohort in the UK **49.6% male**	**Prospective cohort study** - 4-year follow-up **2 assessments:** - Baseline (ages 6-8) and 4 years later (ages 10-11)	Caregiver	Questionnaire using SDQ	Cutoff of a score ≥ 7 based on hyperactivity/ inattention subscale	Overall persistence: 75.5% **Persistence was computed based on reported values in text (i.e., 371 participants had abnormal ADHD at baseline and 5.9% of sample had ADHD at both time points).*	-
Stevens 2008 [43]	**Community sample (N= 217)** - 165 Romanian children adoptees who experienced Ceausescu regime and endured severe institutional deprivation + 52 control adoptees in UK **50% male**	**Prospective cohort study** - 5-year follow-up **2 assessments** - Ages 6 and 11	Caregiver and teacher (both informants' endorsement)	Questionnaire using Revised Rutter Parent and Teacher Scales	Having symptom scores above 1.4 cutoff	52%	-
Clinical sample							
Murray 2017 [11]	**Clinical sample (N= 55)** - Participants recruited through an ADHD Research Clinic at the University of Otago diagnosed	**Prospective cohort study** - 4-year follow-up **2 assessments:** - Baseline (mean age: 7.7) and 4-year follow-up	Caregiver and teacher (endorsed by either of the two)	Questionnaire using the DBDRS	Meeting criteria for DSM-IV for ADHD	61.8%	-

	with ADHD in New Zealand **83.6% male**	(mean age: 11.7)					
Palma 2015 [42]	**Clinical sample (N= 59)** - 37 Participants meeting DSM-IV ADHD at mean age 8.7 + 22 controls - Participants from outpatient facility for neurodevelopment disorders in Brazil **82% male**	**Prospective cohort study** - 4-year follow-up **2 assessments** - Mean age 8.7 and mean age 12-13	Caregiver	Questionnaire using the CBCL	**Syndromatic persistence:** Meeting full DSM-IV criteria for ADHD **Symptomatic persistence:** Meeting subthreshold DSM-IV criteria (more than half of symptoms required for full ADHD diagnosis) **Functional persistence:** Having a score of <18 on GAF scale	**Syndromatic persistence:** 46.4% **Symptomatic persistence:** 35.7% **Functional persistence:** 17.8%	-
Wu 2013 [12]	**Clinical sample (N= 765)** - 499 youths w/ childhood DSM-IV ADHD + 266 controls w/o childhood ADHD - ADHD probands from child psychiatric clinics in Taiwan **71% male**	**Prospective cohort study** - Unknown duration of follow-up **2 assessments** - Baseline and follow-up (mean age: 12.5)	Caregiver and participant (endorsed by either of the two)	Interview using K-SADS-E	Meeting full DSM-IV criteria for ADHD	66.7%	-
Trajectory approach							
Community sample							

Forbes 2017 [44]	**Community sample (N= 2,553)** - Participants from the Longitudinal Study of Australian Children (LSAC)in the Australian Medicare database **52.1% male**	**Prospective cohort study** - 8-year follow-up **5 assessments** - 5 waves every 2 years - Wave 1 (ages 4-5), Wave 5 (ages 12-13)	Caregiver	Questionnaire using SDQ	Continuous score based on 5-item score on the hyperactivity/ inattention subscale	**5 trajectories** 1) Very high increasing (3.7%) **81.3% male** 2) High increasing (9.9%) **70.4% male** 3) Mild (25.4%) **61.2% male** 4) Low (33.4%) **47.9% male** 5) Very low (27.6%) **35.9% male**	-
Jester 2005 [45]	**Community sample (N= 335)** - 225 children of parents with alcoholism + 110 children of parents with no alcoholism in the US **71.0% male**	**Prospective cohort study** - 15-year follow-up **5 assessments** - 5 waves; once every 3 years (ages 3-5 to ages 18-20)	Teacher	Questionnaire using attention problem subscale of the CBCL-Teacher Report Form	Continuous score (range 0-40)	**2 trajectories** 1) High (67.0%) 2) Low (43%)	-
Krasner 2018 [46]	**Community sample (N= 387)** - Participants from regional low birthweight/preterm birth cohort in New Jersey, US **About 50% male**	**Prospective cohort study** - 10-year follow-up **3 assessments** - Ages 6, 9 and 16	Caregiver	Interview using DISC Parent Version	Symptom counts based on DSM-III-R and DSM-IV criteria for ADHD (hyperactivity and inattention symptoms combined)	**3 trajectories** 1) Unaffected (44.2%) 2) School age limited (38.8%) 3) Persistent inattentive (17.1%) *Hyperactivity symptoms declined considerably while inattention symptoms stayed stable.	-
Malone 2010 [47]	**Community sample (N= 754)** - 367 high-risk children (w/	**Prospective cohort study** - 6-year follow-up	Caregiver	Interview using DISC-computerized	Symptom count of DSM-III-R diagnostic	**3 trajectories** 1) Concave (24%) 2) Convex (18%) 3) Minimal (58%)	-

	disruptive behavior problems) + 387 normal children from kindergartens in the US **50% male**	**3 assessments** - 3rd grade, 6th grade, and 9th grade			criteria for ADHD		
Riglin 2016 [48]	**Community sample (N= 9,757)** - Participants from the Avon Longitudinal Study of Parents and Children, a birth cohort study in the UK **About 50% male**	**Prospective cohort study** - 13-year follow-up **7 assessments** - Ages 4 to 17	Caregiver	Questionnaire using SDQ	Dichotomous cutoff based on 7 or more symptom score	**4 trajectories** 1) Low (82.6%) 2) Intermediate (7.7%) 3) Childhood-limited (5.8%) 4) Persistent (3.9%)	-
Sasser 2016 [49]	**Community sample (N= 413)** - Children at high risk for conduct problems - Participants from Fast Track project in the US **66% male**	**Prospective cohort study** - 10-year follow-up **4 assessments** - Grades 3, 6, 9, and 12	Caregiver	Interview using CDISC	Dichotomous cutoff based on 6 or more symptoms threshold for inattention and hyperactivity symptoms	**3 trajectories** 1) Low (71%) - Consistently low levels of inattention and hyperactivity 2) Declining (16%) - Clinically significant inattention and hyperactivity declining below clinical levels 3) High (13%) - Consistent, clinically significant inattention and hyperactivity	-
Shaw 2005 [50]	**Community sample (N= 284)** - Participants from WIC Nutritional	**Prospective cohort study** - 8-year follow-up	Caregiver and teacher (endorsed by either of the two)	Questionnaire using CBCL and CBCL-	Continuous score based on 3 items on hyperactivity/	**4 trajectories** 1) Persistently low (5.7%)	-

	Supplement Programs in the US - Participants were of low income **100% male**	**6 assessments** - Ages 2, 3.5, 5, 6, 8, and 10		Teacher Report Form	inattention problems	2) Moderate desisters (26.9%) 3) Moderately high (47.3%) 4) Chronic (20.0%)	
St Pourcain 2011 [51]	**Community sample (N= 5,383)** - Participants from birth cohort in the UK **49.6% male**	**Prospective cohort study** - 13-year follow-up **7 assessments** - Ages 4, 6, 7, 10, 12, 13, and 17	Caregiver	Questionnaire using SDQ	Cutoff of a score ≥ 7 based on hyperactivity/ inattention subscale	**4 trajectories** 1) Persistently impaired with high probability (3.94%) 2) Intermediate probability (8.07%) 3) Childhood-limited expression (5.25%) 4) Low-risk group (82.75%)	-
van Lier 2007 [52]	**Community sample (N= 316)** - Participants from elementary/high schools in Quebec, Canada **52% male**	**Prospective cohort study** - 5-year follow-up **6 assessments** - Ages 6 to 10 annually	Teacher	Questionnaire using SBQ	Continuous score on the hyperactivity and inattention subscales	**3 trajectories** 1) High (7%) **- 91% male** 2) Intermediate (32%) **- 67% male** 3) Low (61%) **- 41% male**	-
Yilmaz 2017 [53]	**Community sample (N=2,315)** - Twins from the TCHAD study in Sweden **49.4% male**	**Prospective cohort study** - 8-year follow-up **3 assessments** - Ages 8-9, 13-14, 16-17	Caregiver	Questionnaire using a 14-item DSM-IV checklist	Continuous score based on 8 hyperactivity-impulsivity and 6 inattention items	**4 trajectories** 1) Low inattention and low hyperactivity (72.5%) 2) High inattention and low hyperactivity (4.7%) 3) Low inattention and high hyperactivity (1.2%) 4) High inattention and high	-

						hyperactivity (21.6%)	

Table 2.1b. Studies reporting the persistence of hyperactivity symptoms and subsequent smoking outcomes

Reference	Sample type	Study design	Main informant source	Assessment strategy	Definition of hyperactivity	Description of persistence	Smoking outcomes
Proportion approach							
Community sample							
Lambert 1987 [13]	**Community sample (N= 117)** - 59 boys with medically identified DSM-II hyperactivity (that had lasted for at least 2 years) + 58 control boys born in 1960-1965 and who had reached age 12 in Spring 1978 in the US **100% male**	**Prospective cohort study** - 7-year follow-up **2 assessments** - Baseline and 7 years later (mean age: 7.7 to mean age: 14.3)	Caregiver	Interview using a standard interview procedure	Reports of learning, behavior or emotional difficulties; and/or treatment intervention;	47% reported to have persistent learning, behavior, or emotional difficulties 43% reported to have learning, behavior, or emotional difficulties, **AND** still being treated for hyperactivity	-
Trajectory approach							
Community sample							
Côté 2002 [55]	**Community sample (N= 1,569)** - Kindergarten children from public schools in Quebec, Canada - 33.5% participants scored at 80+ percentile on disruptive behaviors **47.7% male**	**Prospective cohort study** - 6-year follow-up **7 assessments** - Ages 6 to 12	Teacher	Questionnaire using SBQ	Continuous score on the hyperactivity subscale	**4 trajectories** **Male:** 1) Highest (36.5%) 2) Declining (35.8%) 3) No hyperactivity (16.9%) 4) Slightly increasing (10.9%) **Female:** 1) No hyperactivity (35.9%) 2) Declining (25.3%) 3) Low stable (21.0%) 4) Highest (17.8%)	-
Fontaine 2008 [56]	**Community sample (N= 1,390)**	**Prospective cohort study**	Teacher	Questionnaire using SBQ	Continuous score on the	**4 trajectories**	**Nicotine use problems (i.e.,**

	- Kindergarten girls from public schools in Quebec, Canada - 31.9% participants scored at 80+ percentile on disruptive behaviors **0% male**	- 6-year follow-up **7 assessments** - Ages 6 to 12			hyperactivity subscale	1) Moderate declining (30.3%) 2) No hyperactivity (25.5%) 3) Moderate stable (25.3%) 4) High declining (19.0%)	**lifetime diagnosis + ≥1 symptom in past year based on DIS-DSM-III-R interview) at mean age 21.2** **Analyses conducted on high hyperactivity (HH) w/ or w/o high physical aggression (HPA)* HH-HPA: 40.96% HH-only: 40.85% Others: 23.28% p≤0.001; HH-HPA vs others: OR= 2.16, p<0.01 HH-only vs. others: OR= 2.23, p<0.001 HH-HPA vs. HH: OR= 0.97, ns
Larsson 2011 [58]	**Community sample (N=2,405)** - Twins from the TCHAD study in Sweden **54.0% male**	**Prospective cohort study** - 8-year follow-up **3 assessments** - Ages 8-9, 13-14, 16-17	Caregiver	Questionnaire using a 14-item DSM-IV checklist	Continuous score based on 8 hyperactivity-impulsivity items	**2 trajectories** 1) Low (91%) **- 49% male** 2) High/decreasing (9%) **- 58% male**	-
Lee 2017 [59]	**Community sample (N= 1,344)**	**Prospective cohort study**	Caregiver	Questionnaire using ARS	Continuous score based on 9	**3 trajectories** 1) Low (56.1%)	-

	- Elementary school children in South Korea **About 50% male**	- 1-year follow-up **3 assessments** - 5-month intervals (ages 6-8)			hyperactivity items	2) Moderate (31.1%) 3) High (12.8%)	
Murray 2017 [11]	**Community sample (N= 1,571)** - Participants recruited from 56 schools in Zurich, Switzerland **51% male**	**Prospective cohort study** - 8-year follow-up **8 assessments** - Annual assessment between ages 7 and 15	Teacher	Questionnaire using SBQ	Continuous score based on 4 hyperactivity items	**4 trajectories** 1) High stable (8%) 2) High decreasing (13%) 3) Low stable (74%) 4) Low increasing (5%)	-
Murray 2018 [68]	**Community sample (N= 1,571)** - Participants recruited from 56 schools in Zurich, Switzerland **51% male**	**Prospective cohort study** - 8-year follow-up **8 assessments** - Annual assessment between ages 7 and 15	Teacher	Questionnaire using SBQ	Continuous score based on 4 hyperactivity items	**3 trajectories** **Male:** 1) Low stable (63%) 2) High stable (24%) 3) High increasing (13%) **Female:** 1) Low stable (81%) 2) High stable (9%) 3) Concave (10%)	-
Musser 2016 [62]	**Community sample (N= 388)** - Community children recruited from public advertisements in the US - Participants determined to have ADHD at baseline (ages 7-11) per	**Prospective cohort study** - 3-year follow-up **3 assessments** - Annual assessment starting at ages 7-11	Caregiver	Questionnaire using ARS	Continuous score on hyperactivity questions	**4 trajectories** 1) Low (25.0%) 2) Moderate decreasing (26.0%) 3) Remitting (31.7%) 4) Persistent (17.5%)	-

	psychologist evaluations **69.2% male**						
Nagin 1999 [63]	**Community sample (N= 1,037)** - Kindergarten children from public schools in Quebec, Canada - Participants from low socioeconomic areas **100% male**	**Prospective cohort study** - 9-year follow-up **7 assessments** - Ages 6, and annually from 10-15	Teacher	Questionnaire using SBQ	Continuous score on the hyperactivity subscale	**4 trajectories** 1) Moderate desister (45%) 2) High desister (30%) 3) Low (20%) 4) Chronic (6%)	-
Pingault 2013 [86]	**Community sample (N= 1,803)** - Kindergarten children from public schools in Quebec, Canada w/ diagnosis of substance abuse/dependence in early adulthood **45.1% male**	**Retrospective cohort study** - 6-year follow-up **7 assessments** - Ages 6 to 12	Caregiver and teacher (combined)	Questionnaire using SBQ	Continuous score based on 2 hyperactivity items (range 0-4)	**3 trajectories** 1) Low (51.3%) 2) High caregiver only (30.8%) 3) High (17.9%)	**Nicotine abuse or mild, moderate, or severe dependence based on DIS-DSM-III-R interview at ages 19-23 (mean 20.9)** Overall: 30.7% - High caregiver only vs. low traj: OR= 0.81; HR= 0.83; ns - High vs. low traj: OR= 0.74; HR= 0.81; ns **Analyses adjusted for inattention, opposition, anxiety traj, adversity, and sex*
Pingault 2011 [65]	**Community sample (N= 2,000)**	**Prospective cohort study**	Teacher	Questionnaire using SBQ	Continuous score based	**4 trajectories** 1) Low (59.4%)	-

	- Kindergarten children from public schools in Quebec, Canada **50.1% male**	- 6-year follow-up **7 assessments** - Ages 6 to 12			on 2 hyperactivity items (range 0-4)	2) Declining (16.0%) 3) Rising (14.3%) 4) High (10.3%)	
Tsai 2017 [66]	**Community sample (N= 1,281)** - Students in grade 3, 5, and 8 from Northern Taiwan **About 50% male**	**Prospective cohort study** - 1-year follow-up **4 assessments** - 3 cohorts followed up quarterly	Caregiver	Questionnaire using Chinese version of SNAP-IV	Continuous score based on 9 hyperactivity items	**3 trajectories** 1) Intermediate (52.5%) 2) Low (40.6%) 3) High (6.9%)	-
Vergunst 2018 [67]	**Community sample (N= 1,374)** - Children from birth registry and also from the Quebec Longitudinal Study of Child Development (QLSCD), Canada **47.1% male**	**Prospective cohort study** - 16-year follow-up **12 assessments** - Ages (mother reports) 1.5, 2.5, 3.5, 4.5, 5, 6 and 8; (teacher reports) 6, 7, 8, 10, 12, and 13; (participant reports) 10, 12, 13, 15 and 17	Caregiver, teacher, and participant	Interview using items derived from early childhood behavior scale from the Canadian National Longitudinal Study of Children and Youth (incorporates items from CBCL, Ontario Child Health Study Scales, and Preschool Behavior Questionnaire) ; (Ages 15 and 17) Mental Health and Social Inadaptation	Continuous standardized score on a 0-10 scale based on 3 hyperactivity items	**6 trajectories** 1) Group 1 (21.6%) 2) Group 2 (10.7%) 3) Group 3 (20.4%) 4) Group 4 (25.9%) 5) Group 5 “chronic” (16.2%) 6) Group 6 “chronic declining” (5.2%) Trajectories further grouped into: 1) Low (78.6%) 2) High (21.4%) Symptoms generally declined from infancy to adolescence across trajectories	-

				Assessment for Adolescents			
Clinical sample							
Anderson 2011 [54]	**Clinical sample (N= 116)** - 65 participants with autism + 27 broad autism spectrum + 24 non-spectrum disability - Participants referred from agencies for young children with delays in the US **80.7% male**	**Prospective cohort study** - 9-year follow-up **19 assessments** - age 9; then every 4 months between ages 13 and 18)	Caregiver	Questionnaire using Aberrant Behavior Checklist	Continuous score on the hyperactivity subscale	**4 trajectories** 1) Low decreasing (44%) 2) Moderate decreasing (36%) 3) High decreasing (11%) 4) Low (9%)	-
Howard 2015 [87]	**Clinical sample (N= 579)** - Participants diagnosed with childhood ADHD combined subtype at ages 7-9.9 - Participants from Multimodal Treatment Study of Children with ADHD (MTA) in the US **80% male**	**Prospective cohort study** - 8-year follow-up **8 assessments** - Baseline, 3 months, 9 months (mean age: 9.6), 24 months (mean age: 10.4), 36 months (mean age: 11.7), 6 years (mean age: 14.9), and 8 years (mean age: 16.8) after randomization	Caregiver and teacher (composite based on average rating)	Questionnaire using SNAP	Continuous hyperactivity symptom score	**4 trajectories (contingent on substance use [binge drinking and marijuana use] in adulthood)** 1) High improving + Low SU: 30% 2) Low improving + Low SU: 38% 3) Low improving + High SU: 16% 4) High improving + High SU: 15%	-

Table 2.1c. Studies reporting the persistence of inattention symptoms and subsequent smoking outcomes

Reference	Sample type	Study design	Main informant source	Assessment strategy	Definition of inattention	Description of persistence	Smoking outcomes
Trajectory approach							
Community sample							
Larsson 2011 [58]	**Community sample (N=2,405)** - Twins from the TCHAD study in Sweden **54.0% male**	**Prospective cohort study** - 8-year follow-up **3 assessments** - ages 8-9, 13-14, 16-17	Caregiver	Questionnaire using a 14-item DSM-IV checklist	Continuous score based on 6 inattention items	**2 trajectories** 1) Low (86%) **- 48% male** 2) High/ increasing (14%) **- 62% male**	-
Lee 2017 [59]	**Community sample (N= 1,344)** - Elementary school children in South Korea **About 50% male**	**Prospective cohort study** - 1-year follow-up **3 assessments** - 5-month intervals (ages 6-8)	Caregiver	Questionnaire using ARS	Continuous score based on 9 inattention items	**3 trajectories** - Low (53.6%) - Moderate (34.0%) - High (12.4%)	-
Murray 2017 [11]	**Community sample (N= 1,571)** - Participants recruited from 56 schools in Zurich, Switzerland **51% male**	**Prospective cohort study** - 8-year follow-up **8 assessments** - Annual assessment between ages 7 and 15	Teacher	Questionnaire using SBQ	Continuous score based on 4 inattention items	**4 trajectories** 1) High stable (20%) 2) High decreasing (10%) 3) Low stable (63%) 4) Low increasing (7%)	-
Murray 2018 [68]	**Community sample (N= 1,571)** - Participants recruited from 56 schools in Zurich, Switzerland **51% male**	**Prospective cohort study** - 8-year follow-up **8 assessments** - Annual assessment between ages 7 and 15	Teacher	Questionnaire using SBQ	Continuous score based on 4 inattention items	**Male:** **2 trajectories** 1) Low stable (61%) 2) High stable (39%) **Female:** **3 trajectories** 1) Low stable (59%)	-

						2) Moderate stable (31%) 3) High decreasing (10%)	
Musser 2016 [62]	**Community sample (N= 388)** - Community children recruited from public advertisements in the US - Participants determined to have ADHD at baseline (ages 7-11) per psychologist evaluations **69.2% male**	**Prospective cohort study** - 3-year follow-up 3 assessments - Annual assessment starting at ages 7-11	Teacher	Questionnaire using ADHD-RS	Continuous score on inattention questions	**3 trajectories** 1) Low (59.6%) 2) High decreasing (18.4%) 3) High persistent (23.0%)	-
Pingault 2013 [86]	**Community sample (N= 1,803)** - Kindergarten children from public schools in Quebec, Canada w/ diagnosis of substance abuse/dependence in early adulthood **45.1% male**	**Retrospective cohort study** - 6-year follow-up **7 assessments** - Ages 6 to 12	Caregiver and teacher (combined)	Questionnaire using SBQ	Continuous score based on 4 inattention items (range 0-8)	**3 trajectories** 1) Low (41.4%) 2) Medium (33.0%) 3) High (25.7%)	**Nicotine abuse or mild, moderate, or severe dependence based on DIS-DSM-III-R interview at ages 19-23 (mean 20.9)** Overall: 30.7% - Medium vs. low traj: OR= 1.78; HR= 1.61; p<0.001 - High vs. low traj: OR= 2.25; HR= 1.94; p<0.001 **Median age of first symptom**

							of nicotine abuse or mild, moderate, or severe dependence Low: not reached/past age 23 Medium: not reached/past age 23 High: 23 **Analyses adjusted for hyperactivity, opposition, anxiety traj, adversity, and sex*
Pingault 2011 [65]	**Community sample (N= 2,000)** - Kindergarten children from public schools in Quebec, Canada **50.1% male**	**Prospective cohort study** - 6-year follow-up **7 assessments** - Ages 6 to 12	Teacher	Questionnaire using SBQ	Continuous score based on 4 inattention items (range 0-8)	**4 trajectories** 1) Stable low (46.3%) 2) Declining (19.3%) 3) Rising (17.6%) 4) Stable high (16.8%)	-
Robbers 2011 [69]	**Community sample (N= 13,832)** - 12,486 twins from twin registry + 1,346 singletons from municipal registers in the Netherlands **49.3% male**	**Prospective cohort study** - 6-year follow-up **3-4assessments** - Every 2 years; participants needed to be ages 6-12	Teacher	Questionnaire using CBCL-Teacher Report Form	Continuous score based on 20 items on Attention Problems subscale	**3 trajectories** % singletons/twins 1) Stable low **- Boys: 64%-71%** **- Girls: 62%-64%** 2) Low-increasing **- Boys: 15%** **- Girls: 16%-18%** 3) High-decreasing **- Boys: 14%-21%** **- Girls: 20%**	-

Tsai 2017 [66]	**Community sample (N= 1,281)** - Students in grade 3, 5, and 8 from Northern Taiwan **About 50% male**	**Prospective cohort study** - 1-year follow-up **4 assessments** - 3 cohorts followed up quarterly	Caregiver	Questionnaire using Chinese version of SNAP-IV	Continuous score based on 9 inattention items	**3 trajectories** 1) Intermediate (58.5%) 2) Low (29.0%) 3) High (12.5%)	-
Vergunst 2018 [67]	**Community sample (N= 1,374)** - Children from birth registry and also from the Quebec Longitudinal Study of Child Development (QLSCD) in Canada **47.1% male**	**Prospective cohort study** - 16-year follow-up **12 assessments** - Ages (mother reports) 1.5, 2.5, 3.5, 4.5, 5, 6 and 8; (teacher reports) 6, 7, 8, 10, 12, and 13; (participant reports) 10, 12, 13, 15 and 17	Caregiver, teacher, and participant	Interview using items derived from early childhood behavior scale from the Canadian National Longitudinal Study of Children and Youth (incorporates items from CBCL, Ontario Child Health Study Scales, and Preschool Behavior Questionnaire) ; (Ages 15 and 17) Mental Health and Social Inadaptation Assessment for Adolescents	Continuous standardized score on a 0-10 scale based on 3 inattention items	**6 trajectories** 1) Group 1 (8.8%) 2) Group 2 (15.3%) 3) Group 3 (22.9%) 4) Group 4 (32.9%) 5) Group 5 “chronic” (16.4%) 6) Group 6 “chronic declining” (3.8%) Trajectories further grouped into: 1) Low (79.8%) 2) High (20.2%) Symptoms generally remained constant from infancy through adolescence across trajectories	-
Clinical sample							

Howard 2015 [87]	**Clinical sample (N= 579)** - Participants diagnosed with childhood ADHD combined subtype at ages 7-9.9 - Participants from Multimodal Treatment Study of Children with ADHD (MTA), US **80% male**	**Prospective cohort study** - 8-year follow-up **8 assessments** - Baseline, 3 months, 9 months (mean age: 9.6), 24 months (mean age: 10.4), 36 months (mean age: 11.7), 6 years (mean age: 14.9), and 8 years (mean age: 16.8) after randomization	Caregiver and teacher (composite based on average rating)	Questionnaire using SNAP	Continuous inattention symptom score	**4 trajectories (contingent on substance use [binge drinking and marijuana use] in adulthood)** 1) High stable + Low SU: 50% 2) Low stable + Low SU: 16% 3) Low worsening + High SU: 17% 4) High worsening + High SU: 17%	-

Table 2.2a. Summary of results from studies based on the proportion approach, by ADHD, hyperactivity, and inattention

	ADHD		Hyperactivity		Inattention	
	# of studies	**Median (range) %**	**# of studies**	**Median (range) %**	**# of studies**	**Median (range) %**
	8	50.8% (43.8%-75.5%)	1	43.0%	0	-
Study population						
Clinically referred	3	61.8% (46.4%-66.7%)	0	-	0	-
Community	5	49.6% (43.8%-75.5%)	1	43.0%	0	-
Gender						
Males only	0	-	1	43.0%	0	-
Females only	0	-	0	-	0	-
Both genders	8	50.8% (43.8%-75.5%)	0	-	0	-
Informant source						
Caregivers	3 (community samples)	48.0% (43.8%-75.5%)	1	43.0%	0	-
Teachers	0 (community sample)	-	0	-	0	-
Caregivers + Teachers	1 (community sample)	52.0%	0	-	0	-
Caregivers + Participants	1 (community sample)	49.2%	0	-	0	-
Assessment method						
Interviews	3 (community samples)	49.2% (43.8%-49.6%)	1	43.0%	0	-
Questionnaires	2 (community samples)	63.8% (52.0%-75.5%)	0	-	0	-

Note: Because there were considerable differences in study design between certain studies, comparisons were not possible. Results of such studies are shown with a dash "-".

Table 2.2b. Summary of results from studies based on the trajectory approach, by ADHD, hyperactivity, and inattention

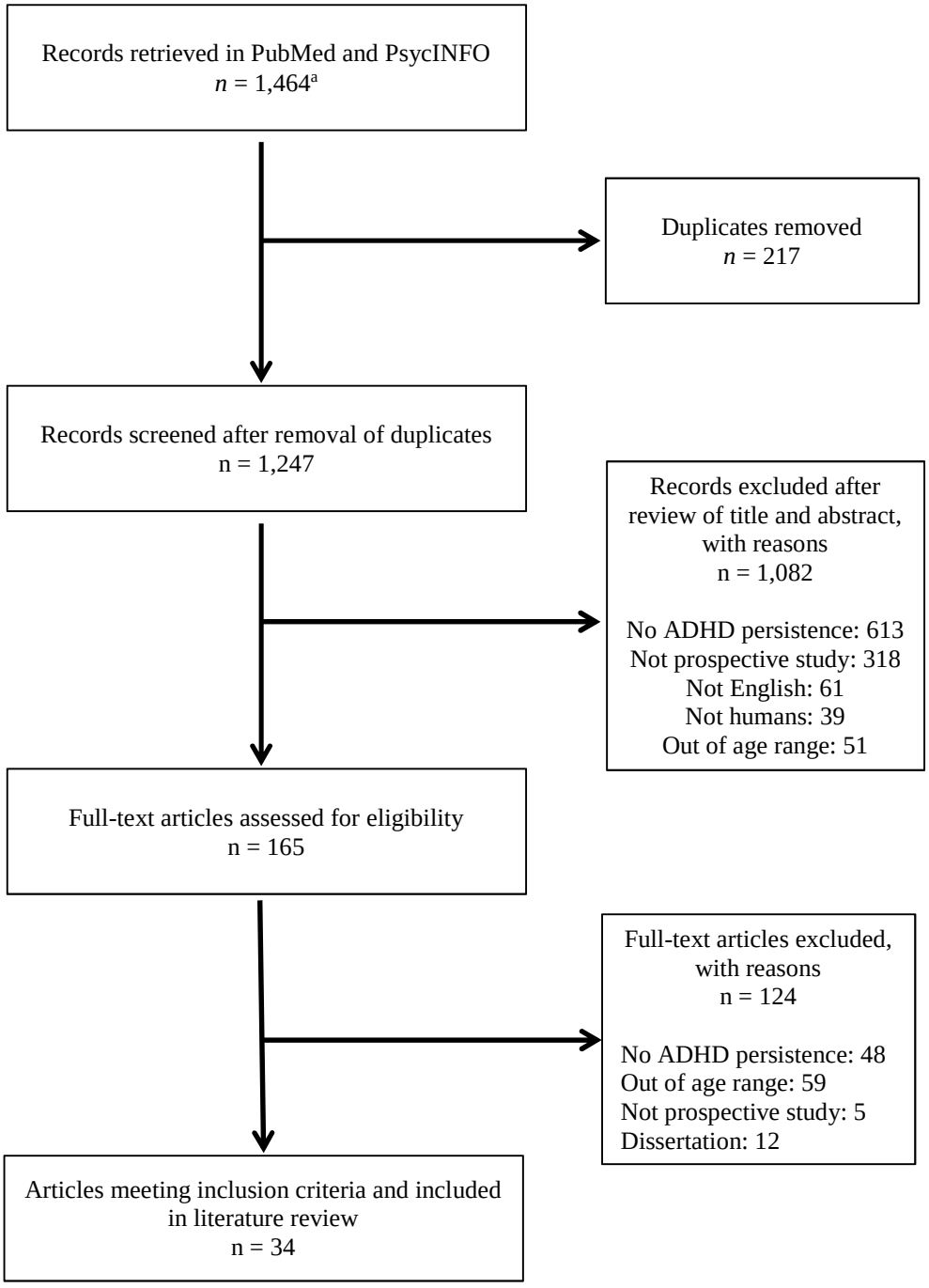
	ADHD		Hyperactivity		Inattention	
	# of studies	**Median (range) # of trajectories**	**# of studies**	**Median (range) # of trajectories**	**# of studies**	**Median (range) # of trajectories**
	10	3.5 (2.0-5.0)	14	4.0 (2.0-6.0)	11	3.0 (2.0-6.0)
	# of studies	**Median (range) %**	**# of studies**	**Median (range) %**	**# of studies**	**Median (range) %**
Commonly reported ADHD trajectories						
Chronically high	4	13.0% (3.9%-21.6%)	-	-	-	-
Chronically moderate	4	7.7% (4.7%-47.3%)	-	-	-	-
Moderate/declining	4	10.9% (1.2%-32.0%)	-	-	-	-
Chronically low	4	71.8% (5.7%-82.8%)	-	-	-	-
Commonly reported hyperactivity trajectories						
Chronically high	-	-	2 (mg, cs)	9.2% (8.0%-10.3%)	-	-
High/declining	-	-	2 (mg, cs)	14.5% (13.0%-16.0%)	-	-
Low/increasing	-	-	2 (mg, cs)	9.7% (5.0%-14.3%)	-	-
Chronically low	-	-	2 (mg, cs)	66.7% (59.4%-74.0%)	-	-
Commonly reported inattention trajectories						
Chronically high	-	-	-	-	3	12.5% (12.4%-18.8%)
Chronically moderate	-	-	-	-	3	34.0% (16.0%-58.5%)
Chronically low	-	-	-	-	3	51.0% (29.0%-65.3%)
Study population						
Clinically referred	0	-	2	-	1	-
Community	10	-	12	-	10	-
Gender						
Males only	1 (4 traj)	High: 20.0% Moderate: 47.3% Mod/decl: 26.9% Low: 5.7%	1 (4 traj)	High: 6.0% High/decl: 30.0%	0	-
Females only	0 (4 traj)	-	1 (4 traj)	High decl: 19.0%	0	-
Both genders	3 (4 traj)	High: 3.9% (3.9%-21.6%) Mod: 7.4% (4.7%-8.1%) Mod/decl: 5.5% (1.2%-32.0%) Low: 77.6% (61.0%-82.8%)	0 (4 traj)	-	11	-

Informant source						
Caregivers	7	-	1 (cs, 3 traj)	<u>Male/Female</u> High: 24.0%/9.0% High inc: 13.0%/10.0% Low: 63.0%/81.0%	1 (cs, 3 traj)	High: 12.5% Mod: 58.5% Low: 29.0%
Teachers	2	-	1 (cs, 3 traj)	High: 6.9% Mod: 52.5% Low: 40.6%	1 (cs, 3 traj)	<u>Male/Female</u> High/decl: 14%-21%/20% Low/inc: 15%/16%-18% Low: 64%-71%/62%-64%
C + T	1	-	1 (cs, 3 traj)	High: 17.9% High (caregiver only): 30.8% Low: 51.3%	1 (cs, 3 traj)	High: 25.7% Mod: 33.0% Low: 41.4%
C + P	0	-	0 (cs, 3 traj)	-	0 (cs, 3 traj)	
C + T + P			0 (cs, 3 traj)	-	0 (cs, 3 traj)	
Assessment method						
Interviews	3	-	1	-	0	-
Questionnaires	7	-	13	-	11	-

Abbreviation: cs=community sample; decl=declining; inc=increasing; mg= mixed gender; mode=moderate; traj=trajectories; C +T=caregivers + teachers; C+P=caregivers + participants; C+T+P=caregivers + teachers + participants.

Note: Because there were considerable differences in study design between certain studies, comparisons were not possible. Results of such studies are shown with a dash "-".

Figure 2.1. Search strategy and method of article selection of literature review



Note:
[a] PsycINFO search yielded 471 records, and PubMed search yielded 993 records.

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CHAPTER 3

Trajectories of hyperactivity and inattention symptom scores in boys of low socioeconomic status and their associated risk factors

ABSTRACT

Background: Recent studies indicate that hyperactivity and inattention symptoms may wax and wane over time. Little is known about symptom score trajectories in risk groups, such as boys from low socioeconomic status (SES) areas, or about the impacts of informant source or risk factors on symptom score trajectories.

Objective: This study derived trajectories of hyperactivity and inattention symptom scores from symptom ratings by teachers and mothers separately, and evaluated risk factors for high symptom score trajectories in a sample of low SES boys.

Method: In a cohort of 1,037 low SES boys, teachers rated boys' hyperactivity and inattention symptoms at age 6 (baseline) and teachers and mothers rated them annually at ages 10-15. Latent class growth analyses were conducted to construct hyperactivity and inattention symptom trajectories, using teacher and mother ratings separately. Potential risk factors for symptom trajectories, including parental/familial factors and boys' baseline behavioral symptoms, were assessed using multivariable regression models.

Results: For both symptom domains, symptom scores followed three trajectories that differed by baseline scores, with a declining trend over time for hyperactivity (high declining, moderate declining, low declining) and a relatively stable trend for inattention (high stable, moderate stable, low stable). About one-fifth and one-third of the boys presented with high hyperactivity scores and high inattention scores, respectively. Mothers concluded similar trends for symptoms trajectories as teachers, but were more likely to rate boys as having high, although not extreme high, scores. Boys' baseline hyperactivity/inattention, opposition, anxiety symptom scores were strong risk factors for both high hyperactivity and inattention trajectories. Associations with family intactness were partially mediated by boys' baseline behavioral symptoms.

Conclusions: The proportion of boys with high symptom score trajectories was higher than boys in general populations, reflecting the at-risk nature of the low SES young male demographic group. Variations in teachers' and mothers' ratings underscore the importance of separate assessments of different informants' ratings. Early behavioral symptoms were strong risk factors for high hyperactivity and inattention trajectories, so was lack of family intactness, which partially conferred its risk via early behavioral problems. Further research is needed on the negative outcomes associated with high symptom trajectories. Analyses of specific, modifiable risk factors could help individuals who might benefit from preventive interventions.

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a neuropsychiatric condition with an estimated prevalence of 7.2% among individuals under the age of 18 years.[1] It is characterized by two symptom domains--hyperactivity/impulsivity and inattention. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), it manifests as one of three subtypes or presentations--predominantly hyperactive-impulsive, predominantly inattentive, and combined, depending on the number of hyperactivity symptoms and/or inattention symptoms.[2] There is considerable literature on the concurrent and longitudinal outcomes of ADHD.[3-15] Compared to children without ADHD, children with ADHD may be at risk for poorer academic performance and are more likely to display externalizing behavioral problems.[3-8] As they enter adolescence and adulthood, children previously diagnosed with ADHD may be less likely to finish high school and more likely to have poor job performance ratings, to be involved in the criminal justice system, and to engage in high-risk behaviors, including unsafe sex and substance use.[9-15]

Once considered a childhood-limited condition, ADHD is now recognized to persist to adolescence and adulthood in about half of the cases.[16-20] Most extant literature has defined and assessed the persistence of ADHD in terms of its presence, based on criteria set by the DSM, at two time points.[16-22] Very few studies have evaluated the persistence of ADHD with reference to its two symptom domains, although available evidence suggests that hyperactivity symptoms tend to decline over time, whereas inattention symptoms remain relatively stable.[23-25]

The past decade has seen increased recognition that the symptoms of ADHD can wax and wane over time, and that their quantity is positively associated with the risk for negative outcomes.[23,26-29] It is therefore inadequate to use just two time points to assess the persistence of

ADHD or to consider ADHD as a dichotomous diagnostic condition. Recent studies have traced the course of ADHD symptoms and symptom domains over multiple time points to characterize the persistence of ADHD more comprehensively.[27,30] These efforts have been facilitated by the use of trajectory analytic methods, such as growth mixed models and latent class growth analysis (LCGA). Recent studies employing such trajectory analytic methods to assess symptom courses of ADHD and, to a lesser extent, hyperactivity and inattention symptoms, have found considerable individual differences in symptom courses within various samples.[31-40] Specifically, some children have persistently high hyperactivity symptom scores, even though the scores decline among most of those with initially high scores.[31,37,38,41-43] The same is true for inattention symptom scores.[31,38,41-43] Depending on the developmental courses of these symptoms, research further indicates that the risks for various behavioral outcomes differ.[36,37,41,42,44]

However, studies vary regarding the number of hyperactivity and inattention symptoms ascribed to children over time and the proportions of children presenting with different symptom scores.[31,41,43,45] Such variation may be, at least in part, attributable to the use of different informants in different studies. Most studies of the developmental courses of ADHD and its symptom domains have relied on one type of informant, typically the children's teachers or parents. Studies using teacher ratings typically find ADHD and its symptom domains to be more persistent and prevalent than do studies based on mother ratings. While studies recognize the validity of both informants' ratings, few studies have directly examined the influence of informant source on symptom persistence.[46]

The current understanding of the symptom courses of hyperactivity and inattention symptoms has largely been based on studies of general, mixed-gender samples.[41,42,44,45,47,48] A few studies have examined symptom courses in special populations, such as individuals with

autism, mania, or disruptive behaviors.[36,37,49,50] However, the literature on other risk groups, such as boys and children of low socioeconomic status (SES), is limited. Male gender is an established risk factor for ADHD. Boys are approximately three times more likely than girls to be diagnosed with the condition,[51-54] and to have higher levels of hyperactivity symptoms. Some but not all studies also support a relationship between male gender and inattention symptoms.[55-57] Low SES is a known risk factor for mental health problems in children,[58] and a growing body of literature suggests that low SES is associated with both hyperactivity and inattention symptoms.[59] One recent study has further suggested that male gender and low SES may interact to confer an additive risk on hyperactivity symptoms.[59] Overall, evidence suggests that boys with low SES are a vulnerable population at high risk for hyperactivity and inattention symptoms. Data on the trajectories of these symptoms are needed to enhance understanding of the overall burden and sequelae of hyperactivity and inattention symptoms over time in this demographic group.

In characterizing individuals most at risk for negative outcomes associated with persistent symptoms of AHD or its symptom domains, some investigators have conducted studies on various risk factors of symptom developmental courses.[31,40,43,45,60] However, most such studies have focused only on a small set of individual characteristics (e.g., temperament [i.e., novelty seeking, harm avoidance, reward dependence, persistence], aggression, and externalizing symptoms) or parental/familial influences; few have accounted for both. Additionally, most studies have assessed these risk factors at the univariate level, and have not accounted for their independent effects or their incremental influences in the presence of other risk factors.

Persistent ADHD can be defined as a diagnosis of ADHD that persists from childhood to adolescence or later. Studies have found disruptive behavioral problems, such as oppositional

defiant disorder and conduct disorder, as well as anxiety disorders in childhood to be predictive of persistent ADHD.[31,61-63] Individuals with persistent ADHD are also more likely to have parents who present with mental disorders, smoke during pregnancy, and to come from families characterized by lower SES and single-parent households, than individuals with remitted ADHD.[62,64,65,66] Research on parental risk factors for persistence has mostly focused on maternal factors, probably because mothers are often the primary caregivers for children and are therefore more available than fathers. Yet, paternal factors may confer additional, independent risks for hyperactivity and inattention symptom trajectories.

In a sample of boys from kindergarten classes in schools of low-income neighborhoods in Montreal, this study aimed: 1) to identify the trajectories of hyperactivity and inattention symptom scores provided by teachers and mothers (separately) from childhood to mid-adolescence; and 2) to assess parental and familial factors, as well as externalizing and internalizing behavioral symptoms in childhood, as potential risk factors for the hyperactivity and inattention symptom score trajectories.

METHODS

Participants

Data were obtained from the Longitudinal and Experimental Study of Low Socioeconomic Status Boys (ELEM).[67] Participants were 1,037 kindergarten boys from 53 schools located in low SES areas (with mean household SES level lower than the provincial norm) in Montreal, Canada, whose kindergarten teachers agreed to participate in the ELEM study; the response rate was 87%. The boys were first identified at an average age of 6.2 years (standard deviation [SD]=0.3) in the fall of 1984. Their teachers evaluated their behavior at that time (the baseline); both their mothers and their teachers did so annually from age 10 through

age 15 years. Each year, the teachers who evaluated the boys were either their sole teacher in that school year or their mathematics or French teacher, who typically had the most contact with the boys.

Measures

The boys' teachers completed the Social Behavior Questionnaire (SBQ) on hyperactivity and inattention symptoms, and other behavioral problems including anxiety and opposition, at baseline, when the boys were age 6 years, and teachers and mothers completed the SBQ annually when the boys were ages 10 through 15 years.[68] The SBQ was based on the Children's Behavior Questionnaire and the Preschool Behavior Questionnaire.[69,70] Its hyperactivity and inattentiveness subscales have demonstrated high reliability and validity in detecting ADHD based on the DSM-III-R diagnostic criteria.[42,71,72]

Hyperactivity and Inattention

Informants (teachers and mothers) rated the boys' hyperactivity and inattention using the hyperactivity subscale and the inattentiveness subscale of the SBQ, respectively. The hyperactivity subscale included two items: a) "restless; runs about or jumps up and down; doesn't keep still," and b) "squirmy, fidgety child." Possible responses for each item were "doesn't apply (0)," "sometimes applies (1)," or "certainly applies (2)." The hyperactivity score represented the sum of the two responses (range 0-4). Based on teacher ratings, a score of 2 or above among boys age 6 years and a score of 1 or above among boys ages 10 years and older represented the 70th percentile of the distribution of boys in the general population of the province.[73,74] For mother ratings, a score of 2 or above among boys ages 10 and 11 years and a score of 1 or above among boys ages 12 years and older represented the 70th percentile.[73,74]

The inattentiveness subscale was composed of four items: a) “has poor concentration or short attention span,” b) “inattentive,” c) “gives up easily,” and d) “stares into space.” Each item was rated on a 3-point scale: “doesn’t apply (0),” “sometimes applies (1),” and “certainly applies (2).” The inattention score was the sum of the four responses (range 0-8). Based on teacher ratings, a score of 3 or above among boys age 6 years and a score of 4 or above among boys ages 10 years and older represented the 70th percentile of the distribution of boys in the general population of the province.[73,74] For mother ratings, a score of 4 or above among boys ages 10 to 12 years and a score of 3 or above among boys ages 13 years and older represented the 70th percentile.[73,74]

We used scores at or above the 70th percentile to define symptom levels as high and to characterize the trajectories identified. In prior trajectory analyses using the SBQ, the 70th percentile has been used to denote high symptom levels and has been found to be a clinically relevant threshold that predicts various cognitive-neuropsychological, academic, and behavioral problems.[36,41,42,75,76] The scores take into account both the number of symptoms and their frequency (i.e., sometimes vs. certainly/constant). Specifically, a hyperactivity symptom score of 2 translates to at least one symptom, whereas a score of 3 or 4 translates to two symptoms, which is the maximum. As for inattention, a symptom score of 3 or 4 translates to at least two symptoms, whereas a score of 5 or 6 translates to at least three symptoms, and a score of 7 or 8 translates to four symptoms, which is the maximum.

To determine the correlation between teacher and mother ratings each year from 10 through 15 years, we used Pearson’s correlations and also consulted current literature. Consistent with what is known about teacher and mother reports, correlation coefficients were low in this study, ranging from 0.20 to 0.35 for hyperactivity scores, and from 0.40 to 0.43 for inattention

scores.[77-82] Current literature indicates a lack of consensus on the best way to integrate different informants' assessments and reveals the limitations of the more commonly proposed integration methods, the "AND" approach and the "OR" approach.[81] The "AND" approach considers a symptom to be present only if both informants agree on its presence, whereas the "OR" approach considers the symptom to be present if either informant endorses it. The former approach is more conservative and decreases the false positive rate, but is also more likely to decrease sensitivity, whereas the latter approach is lenient and increases sensitivity, but at the cost of a higher false positive rate.[81] In light of the low correlations in our data and limitations of common integration approaches suggested by the literature, we concluded that a combined rating would reflect neither the teacher's nor the mother's assessment and would obscure the two informants' separate perspectives. Valo and colleagues, as well as others, such as Bied and colleagues, deem mothers' and teachers' ratings to be valid independently.[46,83] We therefore conducted two separate sets of trajectory analyses based on teacher and mother ratings.

Risk factors

Potential risk factors for the trajectories of hyperactivity symptom and inattention symptom scores included parental and familial risk factors (based on or derived from information provided by the mothers via a questionnaire when the boys were age 6 years), and boys' externalizing and internalizing behavioral scores at baseline (rated by teachers using the SBQ). Parental and familial risk factors included mother's age at the boy's birth, father's age at the boy's birth, mother's occupational prestige, father's occupational prestige, intactness of the family (i.e., two biological parents, single parent, others), parent's depression status (yes in either parent/no in both), parent's anxiety status (yes in either parent/no in both), and mother's use of cigarettes during pregnancy (yes/no). Occupational prestige was a socioeconomic index derived

by Blishen and colleagues and based on an algorithm that incorporated the median employment income of an occupational category and the net proportion of individuals with high education within that occupational category.[84] Parent's depression and anxiety were diagnosed using the Diagnostic Interview Schedule. Boys' externalizing and internalizing behavioral scores included those for opposition, anxiety, inattention (as a potential risk factor for hyperactivity symptom score trajectories), and hyperactivity (as a potential risk factor for inattention symptom score trajectories).

The selection of potential risk factors was guided by existing literature, correlation considerations, and statistical power. Specifically, we first selected potential risk factors with data available in the dataset based on clinical and scientific relevance according to existing literature on the trajectories of hyperactivity and inattention symptoms as well as persistent ADHD. We then constructed a correlation matrix to assess correlations among all potential risk factors. Where the correlation of two variables was more than 0.70, we included only the one of the two deemed more relevant based on literature. In addition, we selected potential risk factors that were composite variables, such as mother's occupational prestige, over their components (e.g., income, mother's years of education) to maximize statistical power in the analyses.

To assess the relationship between the potential risk factors and hyperactivity or inattention symptom score trajectories, we constructed two theoretical frameworks. The first theoretical framework (the "direct effects only framework") assumed only direct paths between the potential risk factors and the symptom score trajectories. The second theoretical framework (the "direct effects and mediation framework") extended the first and assumed that the boys' baseline symptom scores for inattention (for the hyperactivity symptom score trajectory model only), hyperactivity (for the inattention symptom score trajectory model only), opposition, and

anxiety mediate the relationship between some of the other potential risk factors and the symptom score trajectories. The mediational links were first hypothesized based on literature that supports the association between the potential risk factors of interest and the mediators (i.e., baseline symptom scores), as well as between the mediators and either hyperactivity or inattention symptom score trajectories, as shown in Figure 1a and Figure 1b in Appendix 2.[85-88] The associations were then tested using data from the current ELEM database, and associations between the remaining potential risk factors and the mediators were also tested. Associations that were statistically significant, based on a $p<0.05$, were retained in the final theoretical framework, as shown in Figure 3.1a and Figure 3.1b.

Analytic Plan

Consideration of missing data

We assessed the distributions of hyperactivity symptom scores, inattention symptom scores, and the risk factor variables discussed above and checked for outliers and missingness. Most risk factor variables had fewer than 10% missing values. The exceptions (and proportions of missing data) were father's age at the boy's birth (11.3%), mother's (15.3%) and father's occupational prestige (15.8%), parent's depression (30.7%), parent's anxiety (39.2%), and mother's use of cigarettes during pregnancy (58.1%).

In order to enhance the sample size for the analyses, we imputed missing values of risk factors using the multiple imputation procedure and the fully conditional specification method.[89] We conducted five imputations, which yielded five separate imputed datasets for modeling the association between risk factors and trajectory group. Results generated from the five imputed datasets were combined and averaged for valid statistical inference. We did not conduct multiple imputations on the longitudinal data for hyperactivity and inattention scores used to identify

trajectories, because the proc traj procedure in SAS (described further below) automatically utilizes maximum likelihood estimation to account for missing values.

Multiple imputation assumes that data are missing at random (MAR), meaning that missing values should not be systematically different from observed values once observed data are taken into account. For example, if missing values on mother's occupational prestige were lower than observed values, but only because young mothers were less likely to report their own occupational prestige, adjustment of mother's age would minimize bias arising from missingness. To determine the effects of a range of violations of the MAR assumption on the risk factor analyses, we conducted a series of sensitivity analyses. Specifically, we planted a range of bias factors in the multiple imputation procedure, such that the imputed data were systematically inflated or deflated by a percentage from what they would have been if the data were actually MAR. We then conducted a series of risk factor analyses using biased imputed data and identified the "tipping point" at which a risk factor was no longer associated with trajectory group. Lastly, we assessed the plausibility of the bias factor in relation to possible nonrandom missingness.

Trajectory analysis

We constructed the trajectories of hyperactivity symptoms and inattention symptoms using LCGA, and implemented the method using the proc traj procedure in SAS. Unlike common trajectory modeling strategies, such as hierarchical modeling and latent curve modeling, which assume a continuous distribution of trajectories in the population, the LCGA is a semi-parametric group-based trajectory method, as proposed by Nagin,[71] and does not assume any particular type or number of trajectories *a priori*. Limitations of this method include: 1) that

proper estimation of trajectories requires at least three time points, and 2) that identifying the best-fit model (to be described further below) is an iterative process and can be laborious.

To identify the trajectory model that best fit the data, we developed a number of mixture models assuming different numbers of trajectory groups and different orders (i.e., shapes, such as linear, quadratic, or cubic) for the hyperactivity and inattention symptom scores individually, all assuming a censored normal distribution. The model that best fit the data was determined to be the final model. Best fit was determined based on the smallest (i.e., least negative) Bayesian information criterion (BIC), and the largest probability of being the correct model (p_j). p_j was calculated as $\frac{e^{BIC_j - BIC_{max}}}{\sum_j e^{BIC_j - BIC_{max}}}$ where BIC_j was the BIC score of model *j*, and BIC_{max} was the maximum BIC score of all the models under consideration. We also considered parsimony as a complement to the mechanical application of formal statistical criteria. Between any two models under consideration, the model with fewer groups was preferred if the marginal gain in information in the more complex model was minimal and of little clinical relevance. We implemented this subjective step to ensure that the data were not overfitted and that the final model was not far removed from clinical relevance.[90]

We computed and plotted the mean predicted symptom scores and the mean actual symptom scores across all available time points for the trajectories identified in the final model. For ease of visual comparison between symptom score trajectories based on teacher and mother ratings, we did not plot symptom scores assessed at age 6 years by teachers; all symptom score trajectories were plotted using data from ages 10 to 15 years only. Additionally, we computed and plotted the 95% confidence intervals (CIs) associated with the predicted symptom scores of all trajectories.

Risk factors for trajectories

The distribution of parental and familial risk factors and participants' baseline externalizing and internalizing behavioral symptoms was first assessed and compared across the trajectories for hyperactivity symptoms and inattention symptoms, by teacher versus mother rating, using frequencies and proportions for categorical variables and means and standard deviations (SDs) for continuous variables. To evaluate statistical significance, we conducted chi-square tests for categorical variables and ANOVA for continuous variables.

To assess the potential associations of parental and familial risk factors and participants' baseline externalizing and internalizing behavioral symptoms with trajectory group membership for hyperactivity and inattention symptoms, we developed multinomial latent class regression models. We used latent class regression because conventional multinomial logistic regression is based on the assumption that trajectory group membership is fixed and contains no classification error. That assumption does not apply because trajectory groups are probabilistic. A boy's trajectory group assignment is one of several options that is considered most consistent with his behavior, but it is inherently uncertain. The conventional analytic approach does not account for this uncertainty and tends to overstate the statistical significance of observed associations.

Within the direct effects only theoretical framework, we developed four multivariable latent class regression models for hyperactivity or inattention symptom score trajectories, based on either teacher ratings or mother ratings, with all potential risk factors entered simultaneously. We computed model coefficients, standard errors, and their associated odds ratios (ORs) and CIs, using the low symptom score trajectories (to be discussed further below) as referents. Odds ratios associated with high and moderate symptom score trajectories at $p<0.05$ were noted.

To test the direct effects and mediation theoretical framework, treating the boys' baseline symptom scores of inattention, hyperactivity, opposition, and anxiety as potential mediators, we

followed the four-step procedure proposed by Baron and Kenny.[91] The four components of the mediation analysis are illustrated in Figure 3.2. First, we evaluated the total effect of a risk factor on the symptom score trajectories (shown as path ***c*** in the figure) in a multivariable logistic latent class regression, adjusting for other risk factors. Second, we assessed the effect of the risk factor on the mediator (shown as path ***a*** in the figure) in a multivariable linear regression, adjusting for other risk factors. Third, we evaluated the effect of the mediator on the symptom score trajectories conditional on the risk factor (shown as path ***b*** in the figure) using a multivariable logistic latent class regression, adjusting for other risk factors. Fourth, we assessed the direct effect of the risk factor on symptom score trajectories (shown as path ***c'*** in the figure) using a multivariable multinomial latent class regression, adjusting for other risk factors. The presence of mediation was declared if three criteria were met: 1) all relationships assessed in the four steps were statistically significant at $p<0.05$; 2) Sobel test of mediation yielded a $p<0.05$; and 3) the total effect (path ***c)*** and the direct effect (path ***c'***) of the risk factor on the symptom score trajectories was meaningfully different (operationalized in this study as a minimum 10% difference in ORs). If any two or more of the boys' baseline inattention, hyperactivity, opposition, and anxiety symptom scores were found to be independent, statistically significant mediators, we planned to assess for potential joint mediation. To do so, we planned to include all statistically significant component mediators into a joint model as part of the last step of the Baron and Kenny procedure, and to assess the amount of attenuation in the OR estimate of the overall association between risk factor and symptom score trajectory.

RESULTS

At baseline, teachers provided ratings for hyperactivity and inattention symptoms on nearly all 1,037 boys. At age 10 years, 973-977 (93.8%-94.2%) of the boys had teacher ratings,

and 701-702 (67.6%-67.7%) had mother ratings; between ages 11 and 15 years, 753-942 (72.6%-90.8%) had teacher ratings and 621-731 (59.9%-70.5%) had mother ratings. Across all age years, 536-712 (51.7%-68.7%) of the boys had both informants' ratings. Table 1 in Appendix 2 summarizes the number and proportion of boys with teacher, mother, and both ratings for hyperactivity and inattention symptoms across different age years.

Trajectory analysis

Hyperactivity symptom score trajectories

The best fit model for hyperactivity symptoms, based on teacher ratings, was a model with three trajectory groups, all declining over time. Figure 3.3a depicts this three-group model, showing the mean predicted hyperactivity symptom scores (dotted lines) and the mean actual hyperactivity symptom scores (solid lines) of all individuals in each trajectory group observed over time. The grayed area represents symptom scores below the 70th percentile. The estimated proportions of the sample belonging to each group are also presented. Nearly a third of the sample (31.1%) had "low" (0-1) hyperactivity symptom scores at each time point. Nearly half (48.3%) had "moderate" (1-2) symptom scores initially, and their scores gradually declined to low levels during follow-up. About one fifth of the sample (20.6%) had an initially "high" (>2) symptom score at age 6 years; the scores of that group remained high during follow-up, although they gradually declined.

Mother ratings yielded a similar three-group model (low declining, moderate declining, and high declining), although mothers' hyperactivity scores were slightly higher than teachers' scores (e.g., mean scores at age 10 for the high declining trajectory group: mothers'= 3.6, teachers'= 2.8). The estimated proportion of the sample assigned by mothers to the high declining trajectory group was slightly smaller than that assigned by teachers (16.1% vs. 20.6%).

A larger proportion of the sample was identified as belonging to the moderate declining as opposed to the low declining trajectory group by the mothers than by the teachers. Figure 3.3b illustrates the three-group model for hyperactivity symptom scores based on mother ratings.

Figures 2a and 2b in Appendix 2 illustrate the 95% CIs of the predicted values across all time points of the three hyperactivity symptom score trajectories based on teacher ratings and mother ratings, separately. As the plots show, the three sets of 95% CIs do not overlap, suggesting that the trajectories are distinctly different.

Inattention symptom score trajectories

The best fit model for inattention symptom scores based on teacher ratings also generated three trajectory groups, all with relatively stable symptom levels over time. Figure 3.4a depicts this three-group model and the corresponding estimated distribution of the sample by group. A small proportion of the sample (19.0%) had consistently "low" (~1) inattention symptom scores. Approximately 42.1% of the sample had consistently "moderate" (2-4) symptom scores, and the remaining 38.9% had "high" (4-6) symptom scores.

Based on mother ratings, a three-group model comprised of relatively stable trajectories was also identified. Mothers generally scored symptoms higher than did teachers. Inattention symptom scores fell into low, moderate, or high trajectories (Figure 3.4b). Mothers assigned fewer participants to the high symptom score trajectory than did teachers (22.4% vs. 38.9%).

Figures 3a and 3b in Appendix 2 illustrate the 95% CIs of the predicted values across all time points of the three inattention symptom score trajectories based on teacher ratings and mother ratings, separately. The lack of overlap across the three sets of 95% CIs suggests that the trajectories are distinctly different.

Distributions of risk factors across trajectory groups

Hyperactivity symptom score trajectories

Table 3.1a illustrates the distribution of participants' externalizing and internalizing behavioral symptom scores at age 6 years and parental and familial risk factors across the three trajectory groups for hyperactivity symptom scores based on teacher ratings. The mean (standard deviation; SD) hyperactivity symptom score for the high declining trajectory group was 2.8 (1.3), compared with 1.5 (1.4) in the moderate declining trajectory group and 0.5 (0.9) in the low declining trajectory group ($p<0.001$). Compared with the low trajectory group, participants in the high and moderate trajectory groups had higher inattention and opposition symptom scores ($p<0.001$), and were less likely to come from an intact family (64.6% and 74.2%, respectively vs. 81.6% in the low group [$p<0.001$]). Parents of participants belonging to the high and moderate trajectory groups were younger when they gave birth to the participants, had lower occupational prestige compared with the low group, and were more likely to have anxiety (all $p<0.05$). Similar distributions of risk factors were observed for hyperactivity symptom score trajectories based on mother ratings (Table 3.1b).

Inattention symptom score trajectories

Table 3.2a illustrates the distribution of participants' externalizing and internalizing behavioral symptom scores at age 6 as well as parental and familial risk factors across the three trajectory groups for inattention symptom scores based on teacher ratings. The mean (SD) inattention symptom scores were 1.0 (1.4) in the low trajectory group, and 2.3 (2.0) and 3.9 (2.4) in the moderate trajectory group and the high trajectory group, respectively ($p<0.001$). Compared with the low trajectory group, participants in the high trajectory and moderate trajectory group had higher hyperactivity, opposition, and anxiety scores, and were less likely to come from an intact family (all $p<0.05$). The parents of participants belonging to the high trajectory group and

moderate trajectory group had lower occupational prestige than the low trajectory group. The mothers of the high trajectory group and the moderate trajectory group were also younger when they gave birth to the participants ($p<0.05$). Similar distributions of risk factors were observed for the three inattention symptom score trajectories based on mother ratings (Table 3.2b).

Risk factors for trajectory groups

Hyperactivity symptom score trajectories - Direct effects only framework

Table 3.3a presents the results on the multinomial latent class regressions on the risk factors for high and moderate hyperactivity symptom score trajectories based on teacher ratings. Participant's inattention and opposition symptom scores at age 6 years were associated with 1.82- and 2.87-fold higher odds of the high declining trajectory than of the low declining trajectory. Also positively associated with the high declining trajectory was parent's anxiety (OR=6.35). Participant's anxiety (OR=0.55) and family intactness (OR=0.45) were associated with lower odds of the high declining trajectory, as were mother's and father's occupational prestige, although the magnitude of the association with occupational prestige was small (both ORs= 0.96).

Table 3.3b presents results from the multinomial latent class regression based on mother ratings. Fewer risk factors were associated with the high declining trajectory. Only the boys' inattention and opposition symptom scores were (positively) associated with the high trajectory group (OR=1.19 and 1.13, respectively).

Hyperactivity symptom score trajectories - Direct effects and mediation framework

Tables 3.3d-e present results of the three sets of analyses of symptom scores for inattention, opposition, and anxiety at age 6 years as potential mediators of the association between various risk factors and hyperactivity symptom score trajectories based on teacher

ratings. Coefficients, ORs and 95% CIs obtained from the assessments of the four-step procedure proposed by Baron and Kenny are shown.

Of the three potential mediators assessed, only boys' opposition symptom score at age 6 years was found to mediate the association between family intactness and high declining hyperactivity symptom score trajectory based on teacher ratings. The data satisfied all criteria of all four steps of the Barron and Kenny procedure for mediation. Specifically, the Step 1 criterion was demonstrated by the overall association of family intactness with high declining trajectory (OR=0.38, $p<0.001$), indicating that boys from intact families were at lower odds of following a high declining hyperactivity symptom score trajectory than boys from non-intact families. Step 2 of the criterion was demonstrated by the association of family intactness with opposition symptom score at age 6 years. Mean opposition symptom score at age 6 years was -0.97 lower among boys from intact families than those of boys from non-intact families (all $p<0.05$). Step 3 of the criterion was also met: the associations of the baseline behavioral symptom scores and the high declining hyperactivity symptom score trajectory were all statistically significant (opposition: OR= 2.70, $p<0.001$). Step 4 of the criterion was shown by the direct association of family intactness with high declining hyperactivity symptom score trajectory, adjusting for opposition symptom score at age 6 years (OR=0.52, $p=0.047$).

The Sobel test statistic for mediation indicated the mediation effects of opposition symptom score at age 6 years was statistically significant ($Z=-4.44$, $p<0.001$). The association between family intactness and high declining hyperactivity symptom score trajectory was attenuated by 37% after adjusting for opposition symptom score at age 6 years.

None of the mediational analysis results for hyperactivity symptom score trajectories based on mother ratings reached statistical significance, as shown in Tables 3.3f-h

Inattention symptom score trajectories - Direct effects only framework

Table 3.4a presents the multinomial latent class regression models of the risk factors for inattention symptom score trajectory groups based on teacher ratings. Participant's hyperactivity (OR=1.84), opposition (OR=1.33), and anxiety (OR=1.14) at baseline as well as parent's anxiety (OR=2.71) were linked to higher odds of the high trajectory compared with the low trajectory. Family intactness (OR=0.38) was associated with lower odds of the high trajectory. Mother's age at the birth of the participant, and mother's and father's occupational prestige were also associated with lower odds of the high trajectory, although the magnitude of the association was small (ORs ranged between 0.90 and 0.97).

Table 3.4b presents the multinomial latent class regression models for inattention symptom score trajectory groups based on mother ratings. Participant's hyperactivity (OR=1.39) and parent's anxiety (OR=2.89) were the only two risk factors associated with the high trajectory.

Inattention symptom score trajectories - Direct effects and mediation framework

Tables 3.4c-e present results of the three sets of analyses of participant's hyperactivity, opposition, and anxiety symptom scores at age 6 years as potential mediators of the association between various risk factors and inattention symptom score trajectories based on teacher ratings. Coefficients, ORs and 95% CIs obtained from the assessments of the four-step procedure proposed by Baron and Kenny are shown.

Participant's hyperactivity and opposition symptom scores at age 6 years mediated the association between family intactness and high trajectory based on teacher ratings. All criteria of the four steps of the Barron and Kenny procedure for mediation were satisfied. For Step 1, the OR was 0.25 ($p<0.001$) for the overall association of family intactness with high inattention

symptom score trajectory, suggesting that boys from intact families had lower odds of following a high inattention symptom score trajectory than boys from non-intact families. For Step 2, the means of hyperactivity and opposition among boys from intact families at age 6 years were lower ($p<0.001$) than those of boys from non-intact families. For Step 3, baseline behavioral symptom scores were associated with high inattention symptom score trajectory (hyperactivity: OR=2.43, $p<0.001$; opposition: OR=1.68, $p<0.001$). For Step 4, the association between family intactness and high inattention symptom score trajectory, adjusting for hyperactivity symptom score and for opposition symptom score at age 6 years was OR=0.35 ($p=0.004$) and OR=0.34 ($p=0.004$), respectively.

The Sobel test statistic supported the mediation effects of hyperactivity and opposition symptom scores at age 6 years (hyperactivity: Z= -3.98, $p<0.001$; opposition: Z=-3.99, $p<0.001$). The association between family intactness and high inattention symptom score trajectory was attenuated by 38% and 35% after adjusting for hyperactivity and opposition symptom scores at age 6 years, respectively.

Hyperactivity and opposition symptom scores at age 6 years acted as joint mediators on the association between family intactness and high trajectory based on teacher ratings. A separate Step 4 analysis conducted indicated that the association between family intactness and high inattention symptom score trajectory, adjusting for both hyperactivity and opposition symptom scores at age 6 years was OR=0.38 ($p=0.009$), representing a 50% attenuation compared to the unadjusted overall association.

None of the results for inattention symptom score trajectories based on mother ratings reached statistical significance, as shown in Tables 3.4f-h.

<u>Sensitivity analyses: assessment of violations of the MAR assumption</u>

Hyperactivity symptom score trajectories

As mentioned above, because certain risk factors had 10% missing values and were multiply imputed, we conducted tipping point sensitivity analyses to assess the effects of a range of violations of the MAR assumption. Specifically, we planted a number of bias factors in the multiple imputation procedure for risk factors that had >10% missing values and were also statistically significant in the main risk factor analyses, and assessed their effects on the main findings. Tables 2a-2c in Appendix 2 shows sensitivity analyses on risk factors for high hyperactivity symptom score trajectory based on teacher ratings. We did not conduct sensitivity analyses on risk factors for trajectories based on mother ratings, because none of the statistically significant risk factors had considerable missing values.

Mother's occupational prestige was a statistically significant risk factor for high symptom score trajectory based on teacher ratings in the original analysis. When the imputed values of mother's occupational prestige were inflated by a factor of 1.13 (the maximum bias factor possible), such that all imputed values were 13% higher than they would have been if they were MAR, mother's occupational prestige would still remain statistically significant. This suggests that the impact of any violation of MAR would likely be minimal.

Father's occupational prestige lost its statistical significance at a bias factor of 1.31, indicating that if all imputed values had been 31% higher than they were in the original analysis, father's occupational prestige would not have been identified as a risk factor for high symptom score trajectory. This violation of MAR would imply that all fathers with missing occupational prestige information at baseline were more likely to have high prestige occupations. That scenario, however, is likely implausible; individuals in high prestige occupations may be more

inclined to report their occupations than unemployed individuals or those in less prestigious occupations. We therefore expect the impact of a violation of MAR to be minimal.

We identified two tipping point bias factors for parent's anxiety--0.90 and 1.04. This suggests that if mothers who did not provide anxiety data were either 10% less likely or 4% more likely to be (or have spouses who were) anxious than they would have been if their data were MAR, parent's anxiety would not have been identified as a risk factor for high symptom score trajectory. This scenario has some plausibility if mothers who were anxious or had spouses who were anxious were just slightly more or less reluctant to report their anxiety. This presents a potential limitation of the data, suggesting instability of the imputed values for parent's anxiety and its role as a risk factor.

Inattention symptom score trajectories

Tables 3a-3c in Appendix 2 shows sensitivity analyses on risk factors for high inattention symptom score trajectory based on teacher ratings. Mother's occupational prestige lost its statistically significance when its imputed values were inflated by a factor of 1.40, such that all imputed values were 40% higher than they would have been if they were MAR. This suggests that the impact of any violation of MAR would likely be minimal. This violation of MAR would imply that all mothers with missing occupational prestige information at baseline were more likely to have high prestige occupations, which is rather implausible because individuals in high prestige occupations may be more likely than not to report their occupations. We therefore expect the impact of a violation of MAR to be minimal.

Father's occupational prestige lost its statistical significance at a bias factor of 1.20, indicating that if all imputed values had been 20% higher than they were in the original analysis, father's occupational prestige would not have been identified as a risk factor for high symptom

score trajectory. For reasons similar to mother's occupational prestige provided above, this is a rather implausible scenario. The impact of a violation of MAR would likely be minimal.

We identified multiple tipping point bias factors for parent's anxiety--0.99, 1.01, and 1.03. This suggests that if mothers who did not provide anxiety data were either just slightly more or less likely to be (or have spouses who were) anxious than they would have been if their data were MAR, parent's anxiety would not have been identified as a risk factor for high symptom score trajectory. Because of the small magnitudes of the bias factors needed to reverse the original finding, we expect this to be a plausible scenario. This is a potential limitation of the data, calling into question whether parent's anxiety is a true risk factor given the instability of the imputed data.

We conducted a similar sensitivity analysis on parent's anxiety for high inattention symptom score trajectory based on mother ratings. At bias factors of 0.87 and 1.15, parent's anxiety lost its statistical significance as a risk factor. Similar to what was described above, this may reflect a potential limitation of the imputed values for parent's anxiety, and its role as a true risk factor (Table 3d in Appendix 2).

DISCUSSION

Our study utilized LCGA to identify trajectories of hyperactivity and inattention symptom scores between childhood and mid-adolescence in a cohort of boys in low SES areas. This trajectory study is one of the first to target this demographic group and to assess both symptom hyperactivity and inattention symptom score trajectories within it, while providing the perspectives of two informants, participants' teachers and mothers. Both hyperactivity and inattention symptom scores followed three trajectories characterized by different symptom levels: high, moderate, and low. Hyperactivity symptom scores were generally found to decline

over time, whereas inattention scores stayed relatively stable. Although most study participants displayed low symptom score trajectories for both domains, approximately one fifth fell into the high declining trajectory of hyperactivity symptom scores, and approximately one third fell into the high trajectory of inattention symptom scores.

Our study also evaluated a number of parental, familial, and participants' externalizing and internalizing behaviors at age 6 years as risk factors for high symptom score trajectories of both hyperactivity and inattention. The strongest risk factors for assignment to the high symptom trajectory for both hyperactivity and inattention were the boys' behavioral symptom scores and family intactness at baseline. To understand the mechanisms underlying these risk factors, we tested a direct effects and a mediation theoretical framework and found that the risk of high symptom score trajectories associated with family intactness is partially mediated by participants' externalizing and internalizing behavioral symptom scores at age 6.

The proportion of individuals in the high trajectories of hyperactivity or inattention symptom scores in this study was slightly larger than that observed in prior trajectory analyses based on general mixed-gender populations.[42,43] In studies conducted by two separate research investigator teams led by Murray and Pingault in Zurich and Montreal, both using teacher ratings on the SBQ, approximately 10% of mixed-gender participants followed from childhood to mid-adolescence were found to be in high symptom score trajectories for hyperactivity, and approximately 20% of participants fell into the high score trajectories of inattention symptoms.[42,43] The higher prevalence of high symptom score trajectories observed in the current study may be due to its all low SES male sample. In a separate study by Murray and colleagues, symptom score trajectories of hyperactivity and inattention were separately constructed for males

and females observed between ages 7 and 15.[92] A much higher proportion of males were found to exhibit high symptom scores over time (37%) compared to females (9%).[36]

The potential impact of low SES on symptom score trajectories is less clear in the literature due to a dearth of data on low SES populations and of studies on the risk factors for symptom score trajectories of hyperactivity and inattention. A recent study by Vergunst and colleagues of risk factors for hyperactivity and inattention symptom score trajectories, found that low maternal education (a component of SES) was associated with high score trajectories of both hyperactivity and inattention symptoms.[85] In studies on ADHD and its subtypes, mostly conducted in clinically referred samples, low income, low social class, and low SES have been found to be associated with higher likelihood of ADHD and the hyperactive-impulsive subtype, as defined by the DSM.[87,88,93,94] Low SES is also linked to other familial and social risk factors, such as low maternal educational attainment and family stress, which are tied to chronic symptom score trajectories for externalizing behaviors as a whole.[95,96]

Three symptom score trajectories were observed for both hyperactivity and inattention among our study participants, largely consistent with the median number of three to four trajectories observed for the two symptom domains in the literature. Also consistent with the literature is the finding that hyperactivity symptoms generally decline as children age, whereas inattention symptoms stay relatively stable.[42,43,45] The difference in developmental courses between the two symptom domains may be due to children's neurodevelopment and the increased social demands that come with age. As children become adolescents and as the parts of their brains involved in self-control mature, they learn to adapt to societal norms and become more capable of suppressing impulsivity.[97-99] As a result, hyperactivity symptoms tend to dissipate over time. However, as children grow up, the academic demands on them often

increase, and they increasingly need to pay sustained attention to complex tasks. The burden of those demands may exceed the adolescent's capacity for attention.[27]

This study assessed symptom score trajectories of hyperactivity and inattention separately based on teacher and mother ratings and, in so doing, demonstrated the unique perspectives of the two informants. Mothers were more likely than teachers to endorse the presence or frequency of symptoms and generally scored the boys higher than did teachers, but were less likely to assign the highest scores to their sons.

The difference between teacher and mother or, more broadly, caregiver ratings may reflect both informants' unique perspectives and variability in children's behavior in different settings and environments.[100-102] In addition, an informant's rating of a behavioral problem may be influenced by the presence of symptoms of another behavioral problem, such that if a child has a number of oppositional behavioral issues, the informant may inflate the hyperactivity ratings.[103] Furthermore, informant discrepancies may reflect different standards for acceptable behavior in different settings.[104] In light of the differences observed between teachers' and mothers' ratings, we decided to rely on the separate accounts of both informants for a full characterization of the symptom score trajectories of hyperactivity and inattention. As some clinicians and researchers recommend, this study incorporated both informants' ratings but kept them separate.[46,83]

Of the various baseline factors considered in the risk factor assessment of this study, the boys' baseline behavioral symptom scores and family intactness at age 6 years were the strongest correlates of high symptom trajectories for both hyperactivity and inattention.

Hyperactivity and inattention symptom scores were strongly associated with each other; each symptom score increase was associated with more than an 80% increase in the odds of high

symptom score trajectory. Baseline symptom scores of opposition, a well-known risk factor for hyperactivity, were associated with a 2.87-fold increase in the odds of high hyperactivity symptom score trajectory and a 1.33-fold increase in the odds of high inattention symptom score trajectory. These findings are consistent with the literature, particularly with the notion that comorbid disruptive behaviors such as conduct and oppositional defiant problems or disorder may share heritable mechanisms with hyperactivity and inattention.[30,62,105,106,107,108]

An unexpected result was that boys' anxiety was a protective factor for the high declining symptom score trajectory for hyperactivity. Anxiety often co-occurs as a comorbidity, with a prevalence of about 25%, in individuals with ADHD.[109] Previous studies of the persistence of ADHD symptoms have generally found anxiety levels to be a risk factor for persistent ADHD.[30,62] Nevertheless, some recent studies have suggested that anxiety in individuals with ADHD may inhibit impulsivity.[110] Additionally, past studies of the relationship between anxiety and persistent ADHD have rarely adjusted for behavioral symptoms such as oppositional defiant problems. It is possible that the link between anxiety and hyperactivity and inattention symptom score trajectories found in past literature was positively confounded by the presence of other psychiatric conditions.[111]

Among the familial risk factors identified in the study, family intactness was a strong protective factor against both high hyperactivity and high inattention symptom score trajectories. The recent study by Vergunst and colleagues also found an association between family intactness and high symptom score trajectory for hyperactivity, although not for inattention.[85] Specifically, children of non-intact families had 1.55 times higher odds of high hyperactivity symptom scores, than children of intact families, on adjustment for other risk factors. In our study, through mediation analysis, we found that the relationship between family intactness and high symptom

score trajectories was partially mediated by boys' behavioral symptom scores, such that the odds ratio for family intactness was attenuated on adjustment for behavioral symptom scores. This finding further confirms the current understanding of the role of family--a lack of family intactness increases the risk for a range of negative psychological outcomes, including aggression, anti-social behavior and opposition, potentially due to suboptimal family environment and diminished parenting for proper child development.[112-114]

The current study is one of the few that analyzed maternal and paternal factors separately; we found that both maternal and paternal occupational prestige, albeit marginally, were associated with hyperactivity and inattention symptom score trajectories. The associations between these parental and familial factors and hyperactivity and inattention are complex; many of these factors may be confounded by other unknown factors. For instance, given that hyperactivity and inattention symptoms are highly heritable traits, the parents of the boys we studied may well have had similar symptoms, which may have led to their lower educational attainment and subsequent low SES.[115] Research has also indicated that children's hyperactivity and inattention symptoms may negatively influence parental SES by reducing their parents' earnings and relationship stability, possibly because caring for children with such symptoms is stressful.[116]

We found parent's anxiety was a risk factor for both hyperactivity symptom score (based on teacher ratings only) and inattention score trajectories. This is consistent with existing literature, which indicates that children with anxious parents are at increased risk of developing anxiety disorder,[117] a common comorbid condition with ADHD.[109] Additionally, parents with mental health problems are at increased risk of having children with higher ADHD symptoms.[118] Nevertheless, as shown in our sensitivity analysis, there may be considerable instability with the

imputed data for parent's anxiety in this study, such that interpretation of parent's anxiety as a true risk factor in our analysis should be done with caution.

Findings from our study should be interpreted in light of a few limitations. First, the SBQ subscales used in this study measure only the presence and frequency of selected hyperactivity and inattention symptoms and do not account for impairments related to these symptoms. Although many of the boys in the study had high symptom score trajectories, they may not necessarily have had high symptom counts, severity or impairments. The hyperactivity and inattentiveness subscales of the SBQ were not meant to provide clinical diagnoses of ADHD. The available components of the subscales were not an exhaustive reflection of the full set of symptoms typically assessed for ADHD. It is possible that boys found to fall into the low symptom score trajectories may have high levels of other hyperactivity or inattention symptoms not assessed in the current study. The components of the SBQ subscales examined in this study were designed to illustrate the developmental courses of selected symptoms, which may or may not be coupled with impairments. Although impairments were not assessed and were outside the scope of the current work, prior studies have confirmed the convergent validity of the SBQ with the diagnostic DSM-III criteria and found high correlation.[42] Furthermore, high symptom levels on either scale have also been found to be associated with academic and cognitive impairments, suggesting meaningful clinical relevance and distinction of different symptom levels and trajectories.[19,20,24,49,50]

Second, we did not directly assess the clinical implications of the various symptom score trajectories of hyperactivity and inattention in terms of short-term and long-term health outcomes. For instance, ADHD and its symptom domains are known to be associated with increased risk for social, behavioral, and health risks, among which cigarette smoking and

nicotine abuse and dependence are top public health problems. Nevertheless, this study provides the framework by identifying the symptom score trajectories of hyperactivity and inattention, as well as their risk factors, needed for future research on possible adverse outcomes of high symptom score trajectories.[3,4,6,8-10,119-122]

Third, mother ratings of hyperactivity and inattention symptoms were first collected when the participants were 10 years of age, unlike teacher ratings, which included baseline symptom scores at age 6 years. As a result, the trajectory analyses based on mother ratings were based on data for ages 10-15 years only. If symptoms changed between ages 6 and 10, mothers' ratings would not have captured them. Furthermore, given that mother ratings yielded less data than teacher ratings, the paucity of factors found statistically significant in the multivariable regressions may be partly due to less variance and statistical power. Nevertheless, the mother ratings provided an alternative perspective and highlighted the potential influence of situational variability on the developmental paths of hyperactivity and inattention symptom scores.

Fourth, while we were able to assess a number of parental and familial risk factors of symptom score trajectories in this study, such risk factors were collected only at baseline when the boys were age 6 years. It is possible that some of these risk factors, such as family intactness, varied as the boys aged. Yet, because such time-varying data were not collected in ELEM, it is impossible to determine their potential impact on the association of these risk factors with symptom score trajectories. In the case of family intactness, it is difficult to tease out the direction of the association of family intactness over time with high symptom score trajectories. While lack of family intactness may translate to suboptimal family environment and parenting, as discussed earlier, high levels of hyperactivity and inattention symptoms could also put a strain on parental relationships.[123]

Fifth, like many longitudinal studies, our study was missing data for a number of risk factors. In particular, about 25% of the sample was missing data on parents' mental depression and anxiety status, and nearly 60% of the sample lacked data on mother's cigarette use at pregnancy. To compensate, we imputed missing values using the multiple imputation procedure and the fully conditional specification method. We further checked for the impact of potential violations of the MAR assumption in our sensitivity analyses, and concluded that most violations were implausible and would result in minimal change to our main findings. The only exception was parent's anxiety. The imputed values may be unstable, so we advise to interpret this risk factor with caution.

Sixth, we had no data on participants' medication use and therefore could not evaluate the prevalence of medication use or the effect of medication on symptom score trajectories. Nevertheless, it is reasonable to assume that any effect would likely be small, as the national prevalence of prescribed ADHD medication use among children (and also among boys) ages 6-9 years in Canada was low in the early 1990's, estimated to be around 2.0%, according to data from the 1994-1995 National Longitudinal Survey on Children and Youth.[124]

Seventh, findings from this study may not be generalizable to the general population or to females because we evaluated only boys from low socioeconomic areas. However, the generalizability of the current findings to males in other similarly socioeconomically disadvantaged areas may be reasonably good. We believe that selection bias was minimal because the boys were recruited from a large sampling pool of 52 schools in low SES neighborhoods in Montreal, and the response rate of eligible teachers invited to participate in the study when it first started in 1984 was 87%.

Despite its limitations, our study offers insight into the trajectories of hyperactivity and inattention symptom scores and their risk factors among boys in a low SES area. Many of the boys maintained high scores for hyperactivity and inattention symptoms over time, although their hyperactivity symptom scores tended to decline over time. Teachers' and mothers' ratings followed similar but not identical patterns over time, potentially indicating differences in children's behavior in different settings.

Early externalizing and internalizing behavioral symptom scores were associated with high symptom score trajectories of hyperactivity and inattention. Family intactness appeared to protect the children's overall psychological well-being and development. The short-term and long-term sequelae of these high symptom score trajectories, such as their effects on health outcomes later in adolescence and adulthood, were beyond the scope of this study. However, knowledge gained from this study regarding risk factors for high symptom score trajectories could be used in future research to identify individuals who may be at risk for such adverse sequelae. Ultimately, behavioral interventions for children and increased support for non-intact families with children may help reduce high hyperactivity and inattention symptom scores and their adverse health outcomes in high-risk populations, such as boys in socioeconomically disadvantaged areas.

Table 3.1a. Participants' externalizing and internalizing behavioral symptom scores, and parental demographics and mental health characteristics at baseline across hyperactivity trajectories based on teacher ratings

	Total sample N= 1037	Low trajectory N= 325	Moderate trajectory N= 516	High trajectory N= 196	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	0.45 ± 0.85 [0.00]	1.48 ± 1.36 [1.00]	2.76 ± 1.33 [3.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	1.90 ± 2.05 [1.00]	2.76 ± 2.34 [2.00]	3.72 ± 2.29 [4.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	1.17 ± 1.67 [0.00]	2.68 ± 2.48 [2.00]	4.27 ± 2.97 [4.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.99 ± 2.72 [3.00]	2.96 ± 2.62 [2.00]	2.80 ± 2.43 [2.00]	0.900
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	26.11 ± 4.49 [25.70]	25.13 ± 4.68 [24.56]	24.27 ± 4.64 [23.84]	<0.001*
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.80 ± 5.46 [28.24]	28.42 ± 5.44 [27.67]	27.26 ± 6.06 [26.06]	<0.001*
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	40.49 ± 12.47 [40.42]	38.05 ± 12.22 [37.10]	34.96 ± 10.18 [29.98]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	42.05 ± 14.07 [38.35]	38.97 ± 12.44 [35.31]	36.02 ± 10.63 [32.57]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	320 (98.5%)	488 (94.6%)	192 (98%)	
Intact	747 (74.7%)	261 (81.6%)	362 (74.2%)	124 (64.6%)	<0.001*
Not intact	253 (25.3%)	59 (18.4%)	126 (25.8%)	68 (35.4%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	243 (74.8%)	355 (68.8%)	121 (61.7%)	
Yes	186 (25.9%)	55 (22.6%)	96 (27%)	35 (28.9%)	0.338
No	533 (74.1%)	188 (77.4%)	259 (73%)	86 (71.1%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	217 (66.8%)	309 (59.9%)	105 (53.6%)	
Yes	112 (17.7%)	26 (12%)	61 (19.7%)	25 (23.8%)	0.015*
No	519 (82.3%)	191 (88%)	248 (80.3%)	80 (76.2%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	136 (41.8%)	227 (44%)	71 (36.2%)	
Yes	168 (38.7%)	48 (35.3%)	86 (37.9%)	34 (47.9%)	0.196
No	266 (61.3%)	88 (64.7%)	141 (62.1%)	37 (52.1%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.1b. Participants' externalizing and internalizing behavioral symptom scores, and parental demographics and mental health characteristics at baseline across hyperactivity trajectories based on mother ratings

	Total sample N= 1037	Low trajectory N= 547	Moderate trajectory N= 341	High trajectory N= 149	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	1.45 ± 1.45 [1.00]	1.02 ± 1.31 [0.00]	2.10 ± 1.50 [2.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	2.70 ± 2.36 [2.00]	2.23 ± 2.16 [2.00]	3.56 ± 2.33 [3.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	2.54 ± 2.60 [2.00]	1.99 ± 2.29 [1.00]	3.58 ± 2.91 [3.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.90 ± 2.56 [2.00]	2.90 ± 2.62 [2.00]	3.19 ± 2.80 [3.00]	0.568
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	25.17 ± 4.64 [24.74]	25.65 ± 4.74 [25.33]	24.78 ± 4.46 [24.07]	0.078
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.51 ± 5.34 [27.82]	28.18 ± 5.63 [27.56]	28.09 ± 6.29 [27.30]	0.285
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	37.06 ± 11.92 [33.32]	40.66 ± 12.12 [40.42]	37.01 ± 11.96 [34.17]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	38.22 ± 11.79 [34.44]	41.98 ± 14.11 [37.67]	37.71 ± 12.55 [34.45]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	513 (93.8%)	341 (100%)	146 (98%)	
Intact	747 (74.7%)	374 (72.9%)	273 (80.1%)	100 (68.5%)	0.011*
Not intact	253 (25.3%)	139 (27.1%)	68 (19.9%)	46 (31.5%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	342 (62.5%)	260 (76.2%)	117 (78.5%)	
Yes	186 (25.9%)	85 (24.9%)	62 (23.8%)	39 (33.3%)	0.126
No	533 (74.1%)	257 (75.1%)	198 (76.2%)	78 (66.7%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	302 (55.2%)	228 (66.9%)	101 (67.8%)	
Yes	112 (17.7%)	49 (16.2%)	34 (14.9%)	29 (28.7%)	0.007*
No	519 (82.3%)	253 (83.8%)	194 (85.1%)	72 (71.3%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	209 (38.2%)	156 (45.7%)	69 (46.3%)	
Yes	168 (38.7%)	90 (43.1%)	48 (30.8%)	30 (43.5%)	0.039*
No	266 (61.3%)	119 (56.9%)	108 (69.2%)	39 (56.5%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.2a. Participants' externalizing and internalizing behavioral symptom scores, and parents' demographics and mental health characteristics at baseline across inattention trajectories based on teacher ratings

	Total sample N= 1037	Low trajectory N= 191	Moderate trajectory N= 443	High trajectory N= 403	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	0.63 ± 1.04 [0.00]	1.25 ± 1.36 [1.00]	1.93 ± 1.53 [2.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	1.03 ± 1.40 [0.00]	2.29 ± 2.00 [2.00]	3.88 ± 2.39 [4.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	1.18 ± 1.65 [0.00]	2.40 ± 2.52 [2.00]	3.26 ± 2.78 [3.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.25 ± 2.32 [2.00]	2.89 ± 2.65 [2.00]	3.33 ± 2.64 [3.00]	<0.001*
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	26.34 ± 4.66 [25.82]	25.45 ± 4.63 [25.05]	24.56 ± 4.58 [24.15]	<0.001*
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.79 ± 5.13 [28.37]	28.54 ± 5.69 [27.72]	27.86 ± 5.67 [27.25]	0.032*
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	42.92 ± 13.09 [43.80]	38.37 ± 11.81 [38.35]	35.68 ± 11.11 [30.11]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	44.30 ± 15.13 [41.22]	39.66 ± 12.90 [35.47]	36.51 ± 10.42 [33.60]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	188 (98.4%)	427 (96.4%)	385 (95.5%)	
Intact	747 (74.7%)	160 (85.1%)	323 (75.6%)	264 (68.6%)	<0.001*
Not intact	253 (25.3%)	28 (14.9%)	104 (24.4%)	121 (31.4%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	145 (75.9%)	319 (72%)	255 (63.3%)	
Yes	186 (25.9%)	34 (23.4%)	78 (24.5%)	74 (29%)	0.350
No	533 (74.1%)	111 (76.6%)	241 (75.5%)	181 (71%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	125 (65.4%)	280 (63.2%)	226 (56.1%)	
Yes	112 (17.7%)	15 (12%)	48 (17.1%)	49 (21.7%)	0.071
No	519 (82.3%)	110 (88%)	232 (82.9%)	177 (78.3%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	81 (42.4%)	203 (45.8%)	150 (37.2%)	
Yes	168 (38.7%)	23 (28.4%)	80 (39.4%)	65 (43.3%)	0.081
No	266 (61.3%)	58 (71.6%)	123 (60.6%)	85 (56.7%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.2b. Participants' externalizing and internalizing behavioral symptom scores, and parents' demographics and mental health characteristics at baseline across inattention trajectories based on mother ratings

	Total sample N= 1037	Low trajectory N= 228	Moderate trajectory N= 607	High trajectory N= 202	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	0.96 ± 1.28 [0.00]	1.47 ± 1.47 [1.00]	1.70 ± 1.49 [2.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	1.77 ± 1.94 [1.00]	2.74 ± 2.33 [2.00]	3.49 ± 2.41 [3.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	1.76 ± 2.17 [1.00]	2.68 ± 2.70 [2.00]	2.84 ± 2.56 [2.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.75 ± 2.61 [2.00]	2.96 ± 2.63 [2.00]	3.10 ± 2.58 [3.00]	0.233
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	26.39 ± 4.94 [26.01]	24.98 ± 4.58 [24.60]	24.89 ± 4.36 [24.44]	<0.001*
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.74 ± 5.77 [28.05]	28.30 ± 5.37 [27.46]	27.94 ± 5.92 [27.30]	0.221
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	42.07 ± 12.84 [43.59]	36.82 ± 11.67 [32.51]	38.16 ± 11.59 [38.32]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	43.08 ± 14.38 [39.10]	38.40 ± 12.14 [34.84]	37.99 ± 12.14 [33.30]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	227 (99.6%)	575 (94.7%)	198 (98%)	
Intact	747 (74.7%)	184 (81.1%)	420 (73%)	143 (72.2%)	0.042*
Not intact	253 (25.3%)	43 (18.9%)	155 (27%)	55 (27.8%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	182 (79.8%)	389 (64.1%)	148 (73.3%)	
Yes	186 (25.9%)	37 (20.3%)	92 (23.7%)	57 (38.5%)	<0.001*
No	533 (74.1%)	145 (79.7%)	297 (76.3%)	91 (61.5%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	159 (69.7%)	338 (55.7%)	134 (66.3%)	
Yes	112 (17.7%)	16 (10.1%)	57 (16.9%)	39 (29.1%)	<0.001*
No	519 (82.3%)	143 (89.9%)	281 (83.1%)	95 (70.9%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	106 (46.5%)	234 (38.6%)	94 (46.5%)	
Yes	168 (38.7%)	33 (31.1%)	101 (43.2%)	34 (36.2%)	0.092
No	266 (61.3%)	73 (68.9%)	133 (56.8%)	60 (63.8%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.3a. Risk factors for hyperactivity symptom score trajectory group based on teacher ratings

Variable	Trajectory group					
	Low declining	Moderate declining		High declining		
Multinomial logit coefficients (SE)						
Constant	-	2.26	(0.97)	3.34	(1.20)	
Boy's inattention at baseline[1]	-	0.31	(0.09)	0.60	(0.10)	
Boy's opposition at baseline[2]	-	0.78	(0.14)	1.06	(0.14)	
Boy's anxiety at baseline[3]	-	-0.33	(0.07)	-0.59	(0.08)	
Mother's age (years) at boy's birth	-	-0.04	(0.04)	-0.09	(0.05)	
Father's age (years) at boy's birth	-	0.02	(0.03)	0.01	(0.04)	
Mother's occupational prestige[4]	-	-0.02	(0.01)	-0.04	(0.02)	
Father's occupational prestige[4]	-	-0.01	(0.01)	-0.04	(0.02)	
Family intactness[5]	-	-0.60	(0.31)	-0.80	(0.38)	
Parent's depression[6]	-	0.07	(0.43)	-0.62	(0.72)	
Parent's anxiety[6]	-	0.70	(0.55)	1.85	(0.79)	
Mother's use of cigarettes during pregnancy[7]	-	0.05	(0.44)	0.31	(0.31)	
Odds ratio (95% CI) of trajectory group of interest versus low declining trajectory group						
Boy's inattention at baseline[1]	-	1.37	(1.16, 1.61) *	1.82	(1.50, 2.21) *	
Boy's opposition at baseline[2]	-	2.18	(1.66, 2.86) *	2.87	(2.17, 3.80) *	
Boy's anxiety at baseline[3]	-	0.72	(0.63, 0.82) *	0.55	(0.47, 0.65) *	
Mother's age (years) at boy's birth	-	0.96	(0.88, 1.05)	0.92	(0.83, 1.01)	
Father's age (years) at boy's birth	-	1.02	(0.95, 1.09)	1.01	(0.93, 1.10)	
Mother's occupational prestige[4]	-	0.98	(0.96, 1.00)	0.96	(0.93, 0.99) *	
Father's occupational prestige[4]	-	0.99	(0.97, 1.01)	0.96	(0.93, 0.99) *	
Family intactness[5]	-	0.55	(0.30, 1.02)	0.45	(0.21, 0.94) *	
Parent's depression[6]	-	1.07	(0.46, 2.50)	0.54	(0.13, 2.22)	
Parent's anxiety[6]	-	2.02	(0.69, 5.95)	6.35	1.35, 29.81) *	
Mother's use of cigarettes during pregnancy	-	1.05	(0.45, 2.49)	1.36	(0.74, 2.49)	

Abbreviation: SE= standard error; CI= confidence interval

[1] Inattention was assessed by teachers when boys were age 6 years using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.

[2] Opposition was assessed by teachers when boys were age 6 years using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.

[3] Anxiety was assessed by teachers when boys were age 6 years using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.

[4] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

[5] Family intacted was assessed based on parents' self report when boys were age 6 years. "Intact" was defined as having two biological parents, "not intact" was defined as having only one parent, and "reconstructed" was defined as having other family structures, including having a step parent, having a guardian, etc.

[6] Parent's depression and anxiety were based on mothers' self report when boys were age 6 years. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.3b. Risk factors for hyperactivity symptom score trajectory group based on mother ratings

Variable	Trajectory group				
	Low declining	Moderate declining		High declining	
Multinomial logit coefficients (SE)					
Constant	-	-1.35	(0.70)	-2.13	(0.93)
Boy's inattention at baseline[1]	-	-0.09	(0.05)	0.17	(0.06)
Boy's opposition at baseline[2]	-	-0.09	(0.04)	0.13	(0.05)
Boy's anxiety at baseline[3]	-	0.09	(0.04)	-0.07	(0.06)
Mother's age (years) at boy's birth	-	0.04	(0.03)	-0.01	(0.04)
Father's age (years) at boy's birth	-	-0.03	(0.03)	0.02	(0.03)
Mother's occupational prestige[4]	-	0.02	(0.01)	0.00	(0.01)
Father's occupational prestige[4]	-	0.02	(0.01)	-0.01	(0.01)
Family intactness[5]	-	0.24	(0.23)	0.04	(0.28)
Parent's depression[6]	-	-0.02	(0.33)	0.28	(0.41)
Parent's anxiety[6]	-	-0.16	(0.42)	0.39	(0.45)
Mother's use of cigarettes during pregnancy[7]	-	-0.42	(0.29)	0.25	(0.25)
Odds ratio (95% CI) of trajectory group of interest versus low declining trajectory group					
Boy's inattention at baseline[1]	-	0.91	(0.82, 1.02)	1.19	(1.05, 1.35) *
Boy's opposition at baseline[2]	-	0.91	(0.84, 1.00) *	1.13	(1.03, 1.25) *
Boy's anxiety at baseline[3]	-	1.10	(1.01, 1.19) *	0.93	(0.83, 1.04)
Mother's age (years) at boy's birth	-	1.04	(0.98, 1.10)	0.99	(0.92, 1.07)
Father's age (years) at boy's birth	-	0.97	(0.92, 1.02)	1.02	(0.96, 1.09)
Mother's occupational prestige[4]	-	1.02	(1.00, 1.03) *	1.00	(0.98, 1.02)
Father's occupational prestige[4]	-	1.02	(1.00, 1.03) *	0.99	(0.97, 1.02)
Family intactness[5]	-	1.27	(0.81, 2.00)	1.04	(0.60, 1.81)
Parent's depression[6]	-	0.98	(0.52, 1.86)	1.32	(0.60, 2.93)
Parent's anxiety[6]	-	0.85	(0.38, 1.93)	1.48	(0.61, 3.56)
Mother's use of cigarettes during pregnancy	-	0.65	(0.37, 1.14)	1.28	(0.79, 2.08)

Abbreviation: SE= standard error; CI= confidence interval

[1] Inattention was assessed by teachers when boys were age 6 years using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.

[2] Opposition was assessed by teachers when boys were age 6 years using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.

[3] Anxiety was assessed by teachers when boys were age 6 years using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.

[4] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

[5] Family intacted was assessed based on parents' self report when boys were age 6 years. "Intact" was defined as having two biological parents, "not intact" was defined as having only one parent, and "reconstructed" was defined as having other family structures, including having a step parent, having a guardian, etc.

[6] Parent's depression and anxiety were based on mothers' self report when boys were age 6 years. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.3c. Inattention symptom score as a potential mediator of the association between risk factors and hyperactivity symptom score trajectories based on teacher ratings

Risk factor	Step 1 (Testing path c) Model: Hyp symptom traj = risk factor			Step 2 (Testing path a) Model: Ina symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Hyp symptom traj = Ina symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Hyp symptom traj = Risk factor + ina symptom @ age 6		
	OR	**(95% CI)**	**p-value**	**Coefficient**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Mother's occupational prestige												
Moderate declining	0.99	(0.97,1.01)	0.266	-0.02	(-0.03,-0.01)	0.002	1.29	(1.15,1.44)	0.000	0.99	(0.97,1.01)	0.358
High declining	0.97	(0.95,0.99)	0.005	-0.02	(-0.03,-0.01)	0.002	1.59	(1.41,1.79)	0.000	0.97	(0.95,1.00)	0.029
Father's occupational prestige												
Moderate declining	0.99	(0.97,1.01)	0.180	-0.01	(-0.03,0.00)	0.031	1.29	(1.15,1.44)	0.000	0.99	(0.97,1.01)	0.239
High declining	0.97	(0.95,0.99)	0.007	-0.01	(-0.03,0.00)	0.031	1.59	(1.41,1.79)	0.000	0.97	(0.94,0.99)	0.015
Family intactness												
Moderate declining	0.57	(0.35,0.95)	0.029	-0.42	(-0.76,-0.08)	0.016	1.29	(1.15,1.44)	0.000	0.52	(0.31,0.88)	0.014
High declining	0.38	(0.22,0.64)	0.000	-0.42	(-0.76,-0.08)	0.016	1.59	(1.41,1.79)	0.000	0.39	(0.22,0.68)	0.001
Mother's use of cigarettes during pregnancy												
Moderate declining	0.98	(0.52,1.85)	0.945	0.35	(-0.06,0.75)	0.113	1.29	(1.15,1.44)	0.000	0.93	(0.49,1.75)	0.815
High declining	1.26	(0.80,1.96)	0.317	0.35	(-0.06,0.75)	0.113	1.59	(1.41,1.79)	0.000	1.28	(0.79,2.07)	0.317

Table 3.3d. Opposition symptom score as a potential mediator of the association between risk factors and hyperactivity symptom score trajectories based on teacher ratings

Risk factor	Step 1 (Testing path c) Model: Hyp symptom traj = risk factor			Step 2 (Testing path a) Model: Opp symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Hyp symptom traj = Opp symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Hyp symptom traj = Risk factor + opp symptom @ age 6		
	OR	**(95% CI)**	**p-value**	**Coefficient**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Mother's occupational prestige												
Moderate declining	0.99	(0.97,1.01)	0.266	-0.01	(-0.03,0.00)	0.085	2.08	(1.66,2.61)	0.000	0.98	(0.96,1.00)	0.110
High declining	0.97	(0.95,0.99)	0.005	-0.01	(-0.03,0.00)	0.085	2.70	(2.14,3.41)	0.000	0.96	(0.94,0.99)	0.010
Mother's age at birth of participant												
Moderate declining	0.95	(0.89,1.01)	0.082	-0.03	(-0.08,0.02)	0.209	2.08	(1.66,2.61)	0.000	0.96	(0.89,1.03)	0.268
High declining	0.91	(0.85,0.98)	0.010	-0.03	(-0.08,0.02)	0.209	2.70	(2.14,3.41)	0.000	0.91	(0.84,1.00)	0.047
Father's age at birth of participant												
Moderate declining	1.02	(0.97,1.07)	0.536	-0.01	(-0.06,0.03)	0.571	2.08	(1.66,2.61)	0.000	1.01	(0.96,1.08)	0.659
High declining	1.00	(0.94,1.07)	0.967	-0.01	(-0.06,0.03)	0.571	2.70	(2.14,3.41)	0.000	1.01	(0.94,1.08)	0.850
Father's occupational prestige												
Moderate declining	0.99	(0.97,1.01)	0.180	-0.01	(-0.02,0.01)	0.217	2.08	(1.66,2.61)	0.000	0.99	(0.97,1.01)	0.185
High declining	0.97	(0.95,0.99)	0.007	-0.01	(-0.02,0.01)	0.217	2.70	(2.14,3.41)	0.000	0.96	(0.94,0.99)	0.010
Family intactness												
Moderate declining	0.57	(0.35,0.95)	0.029	-0.97	(-1.33,-0.60)	0.000	2.08	(1.66,2.61)	0.000	0.63	(0.36,1.09)	0.101
High declining	0.38	(0.22,0.64)	0.000	-0.97	(-1.33,-0.60)	0.000	2.70	(2.14,3.41)	0.000	0.52	(0.27,0.99)	0.047

Table 3.3e. Anxiety symptom score as a potential mediator of the association between risk factors and hyperactivity symptom score trajectories based on teacher ratings

Risk factor	Step 1 (Testing path c) Model: Hyp symptom traj = risk factor			Step 2 (Testing path a) Model: Anx symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Hyp symptom traj = Anx symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Hyp symptom traj = Risk factor + anx symptom @ age 6		
	OR	**(95% CI)**	**p-value**	**Coefficient**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Father's occupational prestige												
Moderate declining	0.99	(0.97,1.01)	0.180	-0.01	(-0.03,0.00)	0.038	0.95	(0.88,1.03)	0.231	0.99	(0.97,1.00)	0.164
High declining	0.97	(0.95,0.99)	0.007	-0.01	(-0.03,0.00)	0.038	0.93	(0.85,1.01)	0.073	0.97	(0.94,0.99)	0.006
Family intactness												
Moderate declining	0.57	(0.35,0.95)	0.029	-0.39	(-0.76,-0.01)	0.044	0.95	(0.88,1.03)	0.231	0.56	(0.34,0.93)	0.024
High declining	0.38	(0.22,0.64)	0.000	-0.39	(-0.76,-0.01)	0.044	0.93	(0.85,1.01)	0.073	0.36	(0.21,0.62)	0.000

Table 3.3f. Inattention symptom score as a potential mediator of the association between risk factors and hyperactivity symptom score trajectories based on mother ratings

Risk factor	Step 1 (Testing path c) Model: Hyp symptom traj = risk factor			Step 2 (Testing path a) Model: Ina symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Hyp symptom traj = Ina symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Hyp symptom traj = Risk factor + ina symptom @ age 6		
	OR	(95% CI)	p-value	Coefficient	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Mother's occupational prestige												
Moderate declining	1.02	(1.00,1.04)	0.0215	-0.02	(-0.03,-0.01)	0.0020	0.93	(0.85,1.01)	0.0807	1.02	(1.00,1.03)	0.0370
High declining	1.00	(0.98,1.02)	0.9621	-0.02	(-0.03,-0.01)	0.0020	1.21	(1.10,1.33)	0.0001	1.00	(0.98,1.02)	0.8044
Father's occupational prestige												
Moderate declining	1.02	(1.00,1.03)	0.0525	-0.01	(-0.02,0.00)	0.0581	0.93	(0.85,1.01)	0.0807	1.02	(1.00,1.03)	0.0479
High declining	0.99	(0.97,1.01)	0.5205	-0.01	(-0.02,0.00)	0.0581	1.21	(1.10,1.33)	0.0001	1.00	(0.97,1.02)	0.6803
Family intactness												
Moderate declining	1.32	(0.84,2.06)	0.2298	-0.39	(-0.71,-0.06)	0.0212	0.93	(0.85,1.01)	0.0807	1.30	(0.83,2.03)	0.2573
High declining	0.79	(0.47,1.31)	0.3516	-0.39	(-0.71,-0.06)	0.0212	1.21	(1.10,1.33)	0.0001	0.87	(0.52,1.46)	0.5923
Mother's use of cigarettes during pregnancy												
Moderate declining	0.65	(0.38,1.13)	0.1534	0.39	(0.01,0.77)	0.0576	0.93	(0.85,1.01)	0.0807	0.67	(0.38,1.18)	0.1893
High declining	1.27	(0.80,2.01)	0.3174	0.39	(0.01,0.77)	0.0576	1.21	(1.10,1.33)	0.0001	1.27	(0.79,2.04)	0.3174

Table 3.3g. Opposition symptom score as a potential mediator of the association between risk factors and hyperactivity symptom score trajectories based on mother ratings

Risk factor	Step 1 (Testing path c) Model: Hyp symptom traj = risk factor			Step 2 (Testing path a) Model: Opp symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Hyp symptom traj = Opp symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Hyp symptom traj = Risk factor + opp symptom @ age 6		
	OR	(95% CI)	p-value	Coefficient	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Mother's occupational prestige												
Moderate declining	1.02	(1.00,1.04)	0.0215	-0.01	(-0.03,0.00)	0.0662	0.91	(0.84,0.98)	0.0129	1.02	(1.00,1.04)	0.0355
High declining	1.00	(0.98,1.02)	0.9621	-0.01	(-0.03,0.00)	0.0662	1.18	(1.09,1.29)	0.0001	1.00	(0.98,1.02)	0.9081
Mother's age at birth of participant												
Moderate declining	1.04	(0.98,1.10)	0.1874	-0.03	(-0.08,0.01)	0.1676	0.91	(0.84,0.98)	0.0129	1.04	(0.98,1.10)	0.2006
High declining	0.98	(0.91,1.06)	0.6203	-0.03	(-0.08,0.01)	0.1676	1.18	(1.09,1.29)	0.0001	0.99	(0.92,1.07)	0.8240
Father's age at birth of participant												
Moderate declining	0.97	(0.92,1.02)	0.2403	-0.01	(-0.05,0.03)	0.6653	0.91	(0.84,0.98)	0.0129	0.97	(0.92,1.02)	0.1875
High declining	1.02	(0.95,1.08)	0.6137	-0.01	(-0.05,0.03)	0.6653	1.18	(1.09,1.29)	0.0001	1.02	(0.96,1.08)	0.5676
Father's occupational prestige												
Moderate declining	1.02	(1.00,1.03)	0.0525	-0.01	(-0.02,0.01)	0.3275	0.91	(0.84,0.98)	0.0129	1.02	(1.00,1.03)	0.0506
High declining	0.99	(0.97,1.01)	0.5205	-0.01	(-0.02,0.01)	0.3275	1.18	(1.09,1.29)	0.0001	1.00	(0.97,1.02)	0.6754
Family intactness												
Moderate declining	1.32	(0.84,2.06)	0.2298	-0.94	(-1.30,-0.57)	0.0000	0.91	(0.84,0.98)	0.0129	1.23	(0.78,1.93)	0.3758
High declining	0.79	(0.47,1.31)	0.3516	-0.94	(-1.30,-0.57)	0.0000	1.18	(1.09,1.29)	0.0001	1.01	(0.59,1.74)	0.9693

Table 3.3h. Anxiety symptom score as a potential mediator of the association between risk factors and hyperactivity symptom score trajectories based on mother ratings

Risk factor	Step 1 (Testing path c) Model: Hyp symptom traj = risk factor			Step 2 (Testing path a) Model: Anx symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Hyp symptom traj = Anx symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Hyp symptom traj = Risk factor + anx symptom @ age 6		
	OR	(95% CI)	p-value	Coefficient	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Father's occupational prestige												
Moderate declining	1.02	(1.00,1.03)	0.0525	-0.01	(-0.03,0.00)	0.0302	1.04	(0.97,1.12)	0.2777	1.02	(1.00,1.03)	0.0448
High declining	0.99	(0.97,1.01)	0.5205	-0.01	(-0.03,0.00)	0.0302	1.06	(0.97,1.15)	0.2076	0.99	(0.97,1.02)	0.6373
Family intactness												
Moderate declining	1.32	(0.84,2.06)	0.2298	-0.40	(-0.77,-0.02)	0.0368	1.04	(0.97,1.12)	0.2777	1.33	(0.85,2.09)	0.2115
High declining	0.79	(0.47,1.31)	0.3516	-0.40	(-0.77,-0.02)	0.0368	1.06	(0.97,1.15)	0.2076	0.79	(0.48,1.32)	0.3742

Table 3.4a. Risk factors for inattention symptom score trajectory group based on teacher ratings

Variable	Trajectory group						
	Low	Moderate			High		
Multinomial logit coefficients (SE)							
Constant	-	3.02	(0.96)		3.85	(1.03)	
Boy's hyperactivity at baseline[1]	-	0.25	(0.13)		0.61	(0.13)	
Boy's opposition at baseline[2]	-	0.23	(0.08)		0.28	(0.08)	
Boy's anxiety at baseline[3]	-	0.04	(0.05)		0.13	(0.05)	
Mother's age (years) at boy's birth	-	-0.06	(0.04)		-0.11	(0.04)	
Father's age (years) at boy's birth	-	0.04	(0.03)		0.05	(0.03)	
Mother's occupational prestige[4]	-	-0.03	(0.01)		-0.04	(0.01)	
Father's occupational prestige[4]	-	-0.02	(0.01)		-0.03	(0.01)	
Family intactness[5]	-	-0.91	(0.38)		-0.97	(0.37)	
Parent's depression[6]	-	-0.32	(0.39)		-0.05	(0.41)	
Parent's anxiety[6]	-	0.79	(0.48)		1.00	(0.49)	
Mother's use of cigarettes during pregnancy[7]	-	0.45	(0.38)		0.25	(0.25)	
Odds ratio (95% CI) of trajectory group of interest versus low stable trajectory group							
Boy's hyperactivity at baseline[1]	-	1.28	(0.99, 1.66)		1.84	(1.44, 2.36)	*
Boy's opposition at baseline[2]	-	1.26	(1.07, 1.48)	*	1.33	(1.13, 1.55)	*
Boy's anxiety at baseline[3]	-	1.04	(0.94, 1.15)		1.14	(1.03, 1.26)	*
Mother's age (years) at boy's birth	-	0.94	(0.88, 1.02)		0.90	(0.83, 0.97)	*
Father's age (years) at boy's birth	-	1.04	(0.97, 1.11)		1.05	(0.99, 1.12)	
Mother's occupational prestige[4]	-	0.97	(0.95, 1.00)	*	0.96	(0.94, 0.98)	*
Father's occupational prestige[4]	-	0.98	(0.96, 1.00)		0.97	(0.95, 0.99)	*
Family intactness[5]	-	0.40	(0.19, 0.84)	*	0.38	(0.18, 0.78)	*
Parent's depression[6]	-	0.73	(0.34, 1.56)		0.95	(0.42, 2.14)	
Parent's anxiety[6]	-	2.21	(0.87, 5.61)		2.71	(1.05, 7.02)	*
Mother's use of cigarettes during pregnancy[7]	-	1.57	(0.74, 3.33)		1.29	(0.78, 2.12)	

Abbreviation: SE= standard error; CI= confidence interval

[1] Hyperactivity was assessed by teachers when boys were age 6 years using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.

[2] Opposition was assessed by teachers when boys were age 6 years using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.

[3] Anxiety was assessed by teachers when boys were age 6 years using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.

[4] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

[5] Family intacted was assessed based on parents' self report when boys were age 6 years. "Intact" was defined as having two biological parents, "not intact" was defined as having only one parent, and "reconstructed" was defined as having other family structures, including having a step parent, having a guardian, etc.

[6] Parent's depression and anxiety were based on mothers' self report when boys were age 6 years. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.4b. Risk factors for inattention symptom score trajectory group based on mother ratings

Variable	Trajectory group				
	Low	Moderate		High	
Multinomial logit coefficients (SE)					
Constant	-	2.80	(0.72)	1.02	(0.86)
Boy's hyperactivity at baseline[1]	-	0.12	(0.10)	0.33	(0.10)
Boy's opposition at baseline[2]	-	0.12	(0.06)	0.11	(0.06)
Boy's anxiety at baseline[3]	-	-0.04	(0.04)	0.00	(0.05)
Mother's age (years) at boy's birth	-	-0.06	(0.03)	-0.06	(0.04)
Father's age (years) at boy's birth	-	0.03	(0.03)	0.03	(0.03)
Mother's occupational prestige[4]	-	-0.03	(0.01)	-0.02	(0.01)
Father's occupational prestige[4]	-	-0.01	(0.01)	-0.02	(0.01)
Family intactness[5]	-	-0.23	(0.25)	-0.13	(0.29)
Parent's depression[6]	-	0.01	(0.32)	0.55	(0.41)
Parent's anxiety[6]	-	0.66	(0.46)	1.06	(0.44)
Mother's use of cigarettes during pregnancy[7]	-	0.28	(0.26)	0.24	(0.24)
Odds ratio (95% CI) of trajectory group of interest versus low stable trajectory group					
Boy's hyperactivity at baseline[1]	-	1.12	(0.93, 1.35)	1.39	(1.13, 1.71) *
Boy's opposition at baseline[2]	-	1.12	(1.01, 1.25) *	1.12	(0.99, 1.26)
Boy's anxiety at baseline[3]	-	0.96	(0.89, 1.04)	1.00	(0.91, 1.09)
Mother's age (years) at boy's birth	-	0.94	(0.88, 1.00)	0.94	(0.87, 1.01)
Father's age (years) at boy's birth	-	1.03	(0.97, 1.09)	1.03	(0.97, 1.10)
Mother's occupational prestige[4]	-	0.97	(0.95, 0.99) *	0.98	(0.96, 1.01)
Father's occupational prestige[4]	-	0.99	(0.97, 1.00)	0.98	(0.96, 1.00)
Family intactness[5]	-	0.79	(0.49, 1.29)	0.88	(0.49, 1.55)
Parent's depression[6]	-	1.01	(0.54, 1.89)	1.74	(0.79, 3.85)
Parent's anxiety[6]	-	1.93	(0.78, 4.75)	2.89	(1.22, 6.87) *
Mother's use of cigarettes during pregnancy[7]	-	1.32	(0.79, 2.19)	1.27	(0.80, 2.02)

Abbreviation: SE= standard error; CI= confidence interval

[1] Hyperactivity was assessed by teachers when boys were age 6 years using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.

[2] Opposition was assessed by teachers when boys were age 6 years using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.

[3] Anxiety was assessed by teachers when boys were age 6 years using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.

[4] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

[5] Family intacted was assessed based on parents' self report when boys were age 6 years. "Intact" was defined as having two biological parents, "not intact" was defined as having only one parent, and "reconstructed" was defined as having other family structures, including having a step parent, having a guardian, etc.

[6] Parent's depression and anxiety were based on mothers' self report when boys were age 6 years. Having at least one parent with depression and anxiety constituted a yes response.

Table 3.4c. Hyperactivity symptom score as a potential mediator of the association between risk factors and inattention symptom score trajectories based on teacher ratings

Risk factor	Step 1 (Testing path c) Model: Ina symptom traj = risk factor			Step 2 (Testing path a) Model: Hyp symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Ina symptom traj = Hyp symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Ina symptom traj = Risk factor + hyp symptom @ age 6		
	OR	(95% CI)	p-value	Coefficient	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Mother's occupational prestige												
Moderate	0.97	(0.95,0.99)	0.010	-0.01	(-0.01,0.00)	0.239	1.60	(1.27,2.01)	0.000	0.97	(0.95,0.99)	0.009
High	0.96	(0.93,0.98)	0.000	-0.01	(-0.01,0.00)	0.239	2.43	(1.94,3.03)	0.000	0.96	(0.93,0.98)	0.000
Mother's age at birth of participant												
Moderate	0.93	(0.87,1.00)	0.057	-0.01	(-0.04,0.01)	0.311	1.60	(1.27,2.01)	0.000	0.94	(0.88,1.02)	0.118
High	0.89	(0.84,0.96)	0.002	-0.01	(-0.04,0.01)	0.311	2.43	(1.94,3.03)	0.000	0.90	(0.83,0.97)	0.004
Father's age at birth of participant												
Moderate	1.05	(0.99,1.11)	0.136	-0.01	(-0.04,0.01)	0.221	1.60	(1.27,2.01)	0.000	1.04	(0.97,1.10)	0.260
High	1.04	(0.98,1.11)	0.149	-0.01	(-0.04,0.01)	0.221	2.43	(1.94,3.03)	0.000	1.05	(0.99,1.12)	0.123
Father's occupational prestige												
Moderate	0.98	(0.97,1.00)	0.102	-0.01	(-0.02,0.00)	0.055	1.60	(1.27,2.01)	0.000	0.98	(0.96,1.00)	0.117
High	0.97	(0.95,0.99)	0.001	-0.01	(-0.02,0.00)	0.055	2.43	(1.94,3.03)	0.000	0.97	(0.95,0.99)	0.004
Family intactness												
Moderate	0.32	(0.15,0.68)	0.003	-0.51	(-0.73,-0.29)	0.000	1.60	(1.27,2.01)	0.000	0.37	(0.18,0.77)	0.008
High	0.25	(0.12,0.52)	0.000	-0.51	(-0.73,-0.29)	0.000	2.43	(1.94,3.03)	0.000	0.35	(0.17,0.72)	0.004

Table 3.4d. Opposition symptom score as a potential mediator of the association between risk factors and inattention symptom score trajectories based on teacher ratings

Risk factor	Step 1 (Testing path c) Model: Ina symptom traj = risk factor			Step 2 (Testing path a) Model: Opp symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Ina symptom traj = Opp symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Ina symptom traj = Risk factor + opp symptom @ age 6		
	OR	(95% CI)	p-value	Coefficient	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Mother's occupational prestige												
Moderate	0.97	(0.95,0.99)	0.010	-0.01	(-0.03,0.00)	0.092	1.39	(1.20,1.62)	0.000	0.97	(0.95,0.99)	0.017
High	0.96	(0.93,0.98)	0.000	-0.01	(-0.03,0.00)	0.092	1.68	(1.45,1.94)	0.000	0.96	(0.94,0.98)	0.001
Mother's age at birth of participant												
Moderate	0.93	(0.87,1.00)	0.057	-0.03	(-0.07,0.02)	0.270	1.39	(1.20,1.62)	0.000	0.94	(0.87,1.01)	0.085
High	0.89	(0.84,0.96)	0.002	-0.03	(-0.07,0.02)	0.270	1.68	(1.45,1.94)	0.000	0.90	(0.83,0.97)	0.004
Father's age at birth of participant												
Moderate	1.05	(0.99,1.11)	0.136	-0.02	(-0.05,0.02)	0.418	1.39	(1.20,1.62)	0.000	1.05	(0.98,1.12)	0.154
High	1.04	(0.98,1.11)	0.149	-0.02	(-0.05,0.02)	0.418	1.68	(1.45,1.94)	0.000	1.05	(0.99,1.12)	0.115
Father's occupational prestige												
Moderate	0.98	(0.97,1.00)	0.102	-0.01	(-0.02,0.01)	0.299	1.39	(1.20,1.62)	0.000	0.98	(0.96,1.00)	0.115
High	0.97	(0.95,0.99)	0.001	-0.01	(-0.02,0.01)	0.299	1.68	(1.45,1.94)	0.000	0.97	(0.94,0.99)	0.001
Family intactness												
Moderate	0.32	(0.15,0.68)	0.003	-0.94	(-1.31,-0.56)	0.000	1.39	(1.20,1.62)	0.000	0.39	(0.18,0.82)	0.013
High	0.25	(0.12,0.52)	0.000	-0.94	(-1.31,-0.56)	0.000	1.68	(1.45,1.94)	0.000	0.34	(0.17,0.70)	0.004

Table 3.4e. Anxiety symptom score as a potential mediator of the association between risk factors and inattention symptom score trajectories based on teacher ratings

Risk factor	Step 1 (Testing path c) Model: Ina symptom traj = risk factor			Step 2 (Testing path a) Model: Anx symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Ina symptom traj = Anx symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Ina symptom traj = Risk factor + anx symptom @ age 6		
	OR	**(95% CI)**	**p-value**	**Coefficient**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Father's occupational prestige												
Moderate	0.98	(0.97,1.00)	0.102	-0.01	(-0.03,0.00)	0.083	1.08	(0.98,1.20)	0.129	0.99	(0.97,1.00)	0.131
High	0.97	(0.95,0.99)	0.001	-0.01	(-0.03,0.00)	0.083	1.22	(1.11,1.34)	0.000	0.97	(0.95,0.99)	0.001
Family intactness												
Moderate	0.32	(0.15,0.68)	0.003	-0.37	(-0.76,0.03)	0.069	1.08	(0.98,1.20)	0.129	0.33	(0.15,0.71)	0.004
High	0.25	(0.12,0.52)	0.000	-0.37	(-0.76,0.03)	0.069	1.22	(1.11,1.34)	0.000	0.26	(0.13,0.54)	0.000

Table 3.4f. Hyperactivity symptom score as a potential mediator of the association between risk factors and inattention symptom score trajectories based on mother ratings

Risk factor	Step 1 (Testing path c) Model: Ina symptom traj = risk factor			Step 2 (Testing path a) Model: Hyp symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Ina symptom traj = Hyp symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Ina symptom traj = Risk factor + hyp symptom @ age 6		
	OR	(95% CI)	p-value	Coefficient	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Mother's occupational prestige												
Moderate	0.97	(0.95,0.99)	0.000	-0.01	(-0.02,0.00)	0.166	1.26	(1.08,1.46)	0.003	0.97	(0.95,0.99)	0.001
High	0.98	(0.96,1.00)	0.081	-0.01	(-0.02,0.00)	0.166	1.57	(1.32,1.85)	0.000	0.98	(0.96,1.00)	0.114
Mother's age at birth of participant												
Moderate	0.94	(0.89,1.00)	0.049	-0.01	(-0.04,0.01)	0.297	1.26	(1.08,1.46)	0.003	0.94	(0.89,1.00)	0.070
High	0.93	(0.86,1.00)	0.058	-0.01	(-0.04,0.01)	0.297	1.57	(1.32,1.85)	0.000	0.94	(0.87,1.01)	0.099
Father's age at birth of participant												
Moderate	1.03	(0.98,1.08)	0.314	-0.01	(-0.04,0.01)	0.279	1.26	(1.08,1.46)	0.003	1.03	(0.97,1.09)	0.340
High	1.03	(0.96,1.09)	0.419	-0.01	(-0.04,0.01)	0.279	1.57	(1.32,1.85)	0.000	1.03	(0.96,1.10)	0.399
Father's occupational prestige												
Moderate	0.98	(0.97,1.00)	0.073	-0.01	(-0.02,0.00)	0.048	1.26	(1.08,1.46)	0.003	0.99	(0.97,1.00)	0.090
High	0.98	(0.96,1.00)	0.024	-0.01	(-0.02,0.00)	0.048	1.57	(1.32,1.85)	0.000	0.98	(0.96,1.00)	0.058
Family intactness												
Moderate	0.69	(0.43,1.10)	0.121	-0.52	(-0.72,-0.32)	0.000	1.26	(1.08,1.46)	0.003	0.77	(0.48,1.24)	0.287
High	0.65	(0.38,1.13)	0.128	-0.52	(-0.72,-0.32)	0.000	1.57	(1.32,1.85)	0.000	0.84	(0.48,1.48)	0.546

Table 3.4g. Opposition symptom score as a potential mediator of the association between risk factors and inattention symptom score trajectories based on mother ratings

Risk factor	Step 1 (Testing path c) Model: Ina symptom traj = risk factor			Step 2 (Testing path a) Model: Opp symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Ina symptom traj = Opp symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Ina symptom traj = Risk factor + opp symptom @ age 6		
	OR	(95% CI)	p-value	Coefficient	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Mother's occupational prestige												
Moderate	0.97	(0.95,0.99)	0.000	-0.01	(-0.03,0.00)	0.075	1.16	(1.06,1.26)	0.001	0.97	(0.95,0.99)	0.001
High	0.98	(0.96,1.00)	0.081	-0.01	(-0.03,0.00)	0.075	1.25	(1.14,1.38)	0.000	0.98	(0.96,1.00)	0.127
Mother's age at birth of participant												
Moderate	0.94	(0.89,1.00)	0.049	-0.04	(-0.08,0.01)	0.133	1.16	(1.06,1.26)	0.001	0.94	(0.89,1.00)	0.063
High	0.93	(0.86,1.00)	0.058	-0.04	(-0.08,0.01)	0.133	1.25	(1.14,1.38)	0.000	0.94	(0.87,1.01)	0.081
Father's age at birth of participant												
Moderate	1.03	(0.98,1.08)	0.314	0.00	(-0.05,0.04)	0.823	1.16	(1.06,1.26)	0.001	1.03	(0.98,1.09)	0.280
High	1.03	(0.96,1.09)	0.419	0.00	(-0.05,0.04)	0.823	1.25	(1.14,1.38)	0.000	1.03	(0.97,1.10)	0.355
Father's occupational prestige												
Moderate	0.98	(0.97,1.00)	0.073	-0.01	(-0.02,0.01)	0.364	1.16	(1.06,1.26)	0.001	0.98	(0.97,1.00)	0.076
High	0.98	(0.96,1.00)	0.024	-0.01	(-0.02,0.01)	0.364	1.25	(1.14,1.38)	0.000	0.98	(0.96,1.00)	0.034
Family intactness												
Moderate	0.69	(0.43,1.10)	0.121	-0.95	(-1.32,-0.59)	0.000	1.16	(1.06,1.26)	0.001	0.78	(0.48,1.26)	0.316
High	0.65	(0.38,1.13)	0.128	-0.95	(-1.32,-0.59)	0.000	1.25	(1.14,1.38)	0.000	0.83	(0.47,1.47)	0.527

Table 3.4h. Anxiety symptom score as a potential mediator of the association between risk factors and inattention symptom score trajectories based on mother ratings

Risk factor	Step 1 (Testing path c) Model: Ina symptom traj = risk factor			Step 2 (Testing path a) Model: Anx symptom @ age 6 = risk factor			Step 3 (Testing path b) Model: Ina symptom traj = Anx symptom @ age 6 + risk factor			Step 4 (Testing path c') Model: Ina symptom traj = Risk factor + anx symptom @ age 6		
	OR		p-value	Coefficient		p-value	OR		p-value	OR		p-value
Father's occupational prestige												
Moderate	0.98	(0.97,1.00)	0.073	-0.01	(-0.03,0.00)	0.046	1.00	(0.93,1.07)	0.953	0.98	(0.97,1.00)	0.075
High	0.98	(0.96,1.00)	0.024	-0.01	(-0.03,0.00)	0.046	1.05	(0.96,1.14)	0.290	0.98	(0.96,1.00)	0.026
Family intactness												
Moderate	0.69	(0.43,1.10)	0.121	-0.38	(-0.75,-0.01)	0.042	1.00	(0.93,1.07)	0.953	0.69	(0.43,1.10)	0.121
High	0.65	(0.38,1.13)	0.128	-0.38	(-0.75,-0.01)	0.042	1.05	(0.96,1.14)	0.290	0.67	(0.39,1.16)	0.151

Figure 3.1a. Directed acyclic graph of direct effects and mediation framework for hyperactivity symptom score trajectories

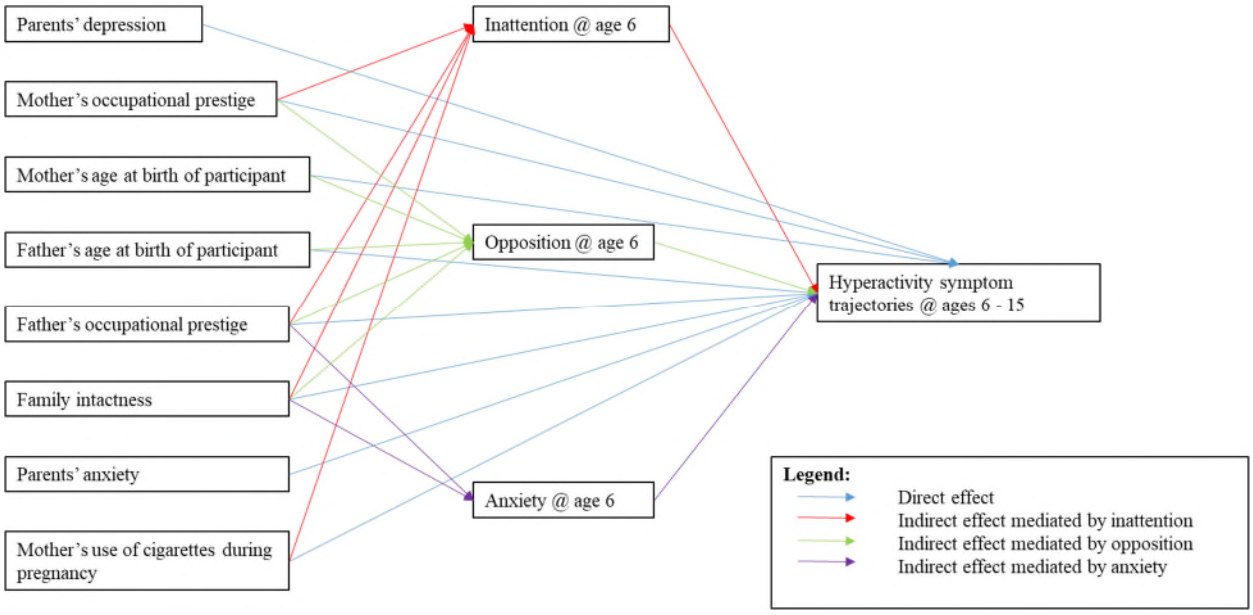


Figure 3.1b. Directed acyclic graph of direct effects and mediation framework for inattention symptom score trajectories

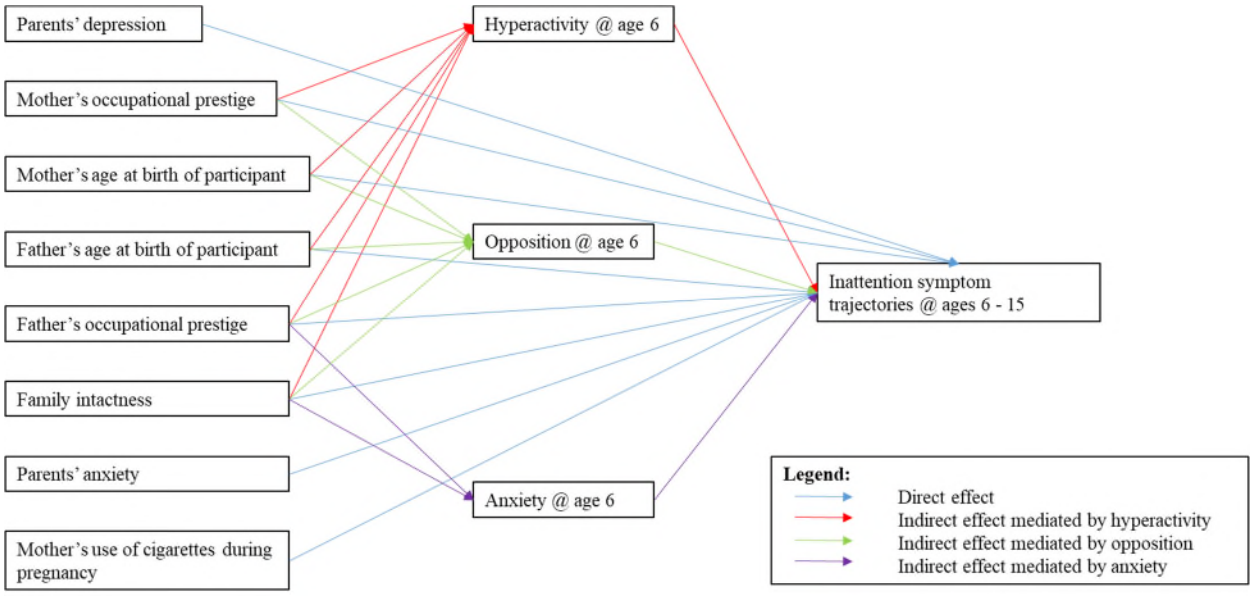


Figure 3.2 Four components of mediation analysis, as proposed by Baron and Kenny[91]

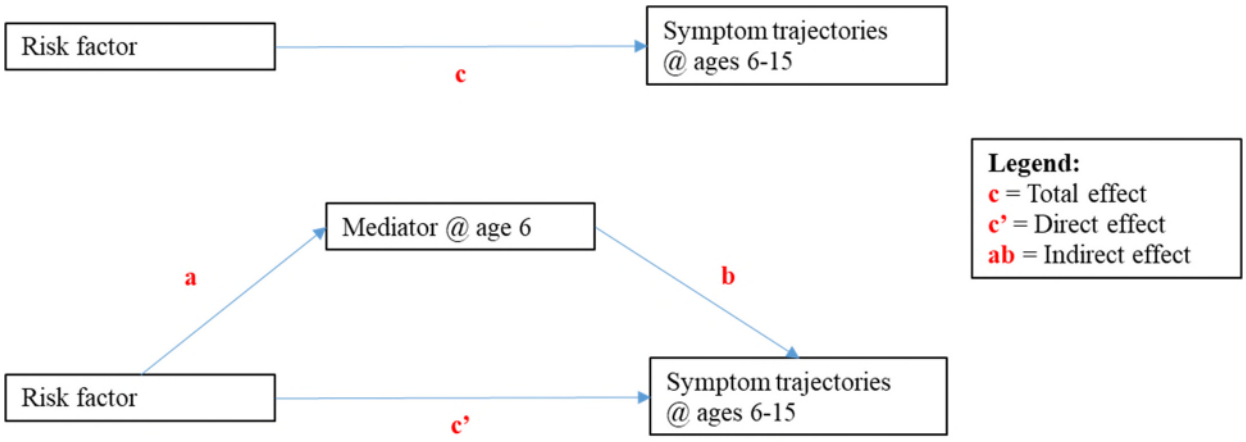


Figure 3.3a. Hyperactivity symptom score trajectories (teacher ratings) - Predicted versus observed trajectories

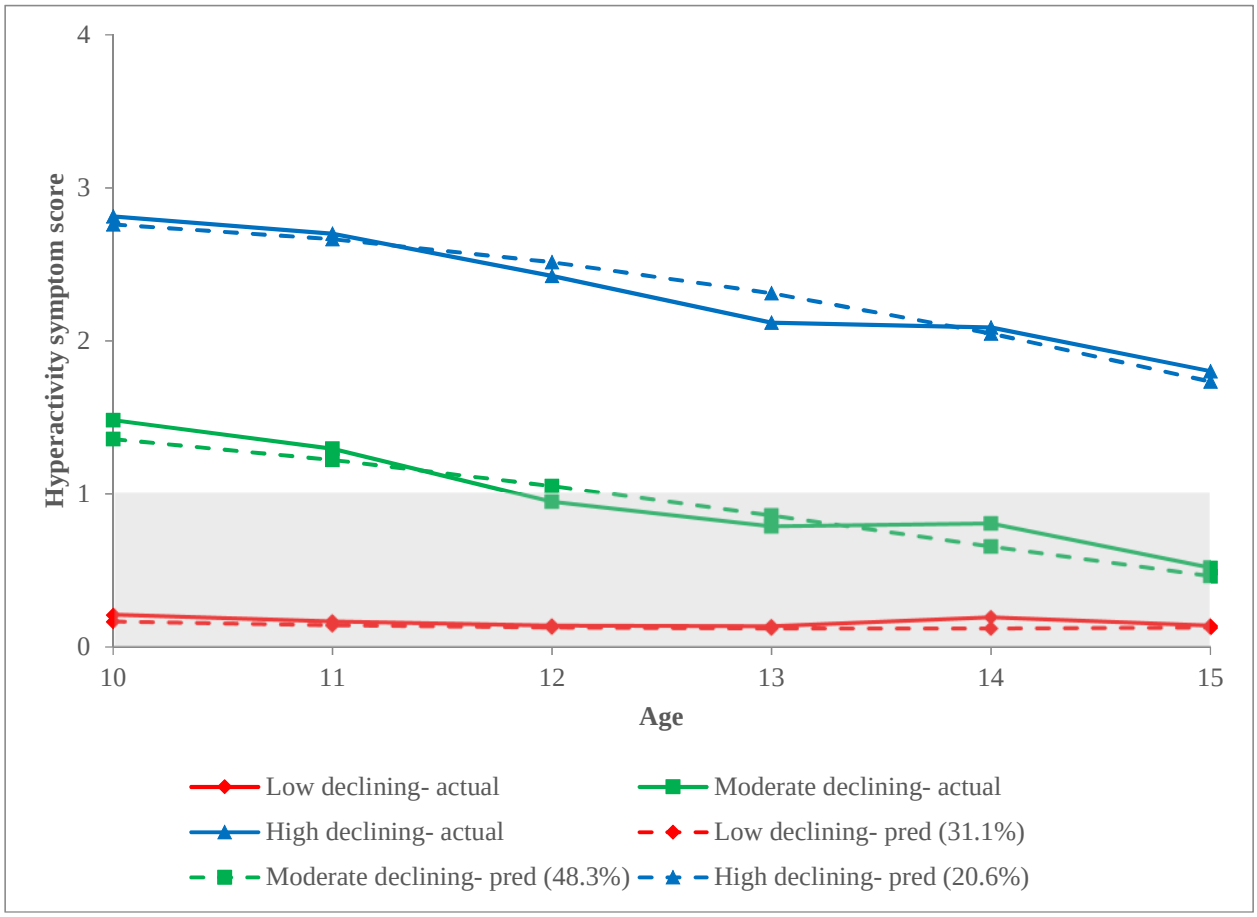


Figure 3.3b. Hyperactivity symptom score trajectories (mother ratings) - Predicted versus observed trajectories

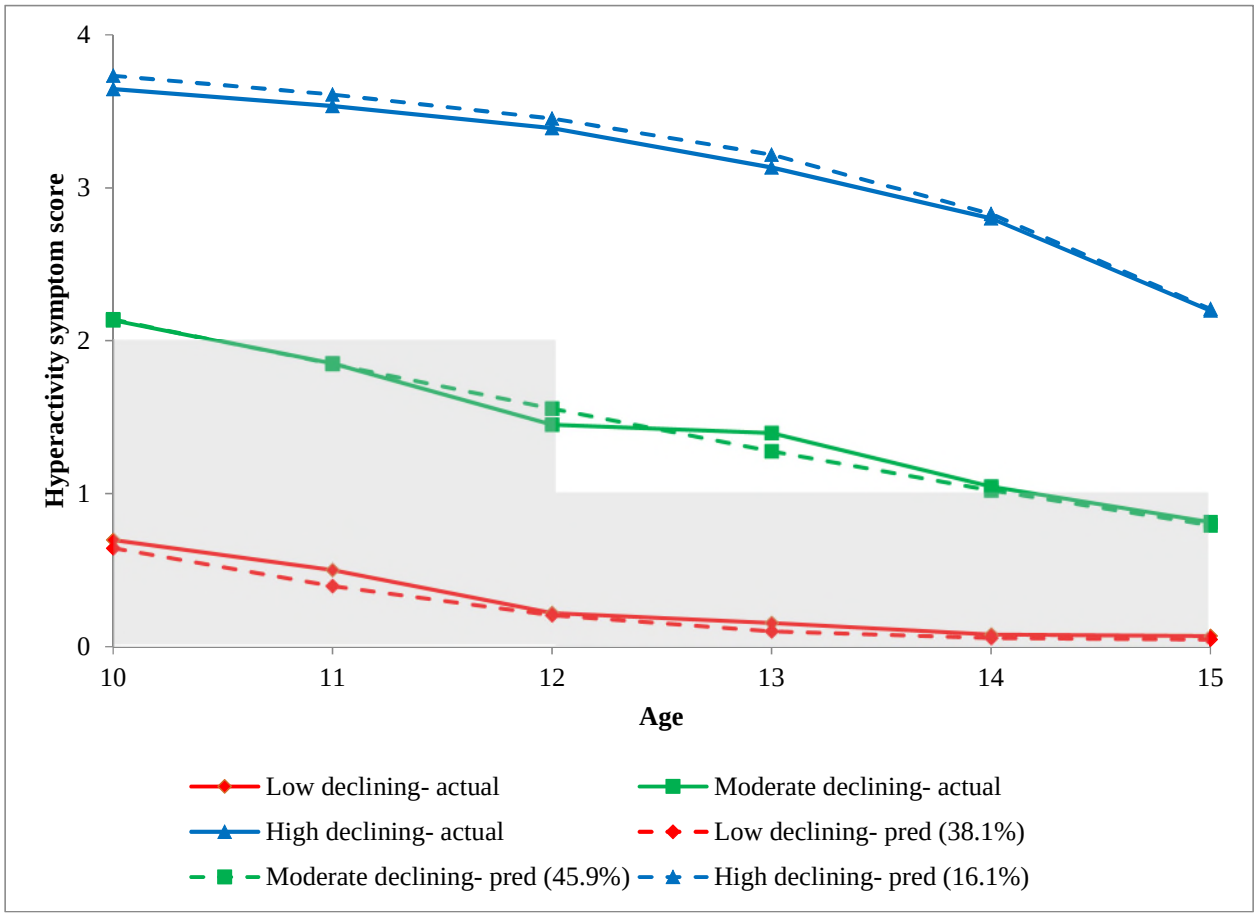


Figure 3.4a. Inattention symptom score trajectories (teacher ratings) - Predicted versus observed trajectories

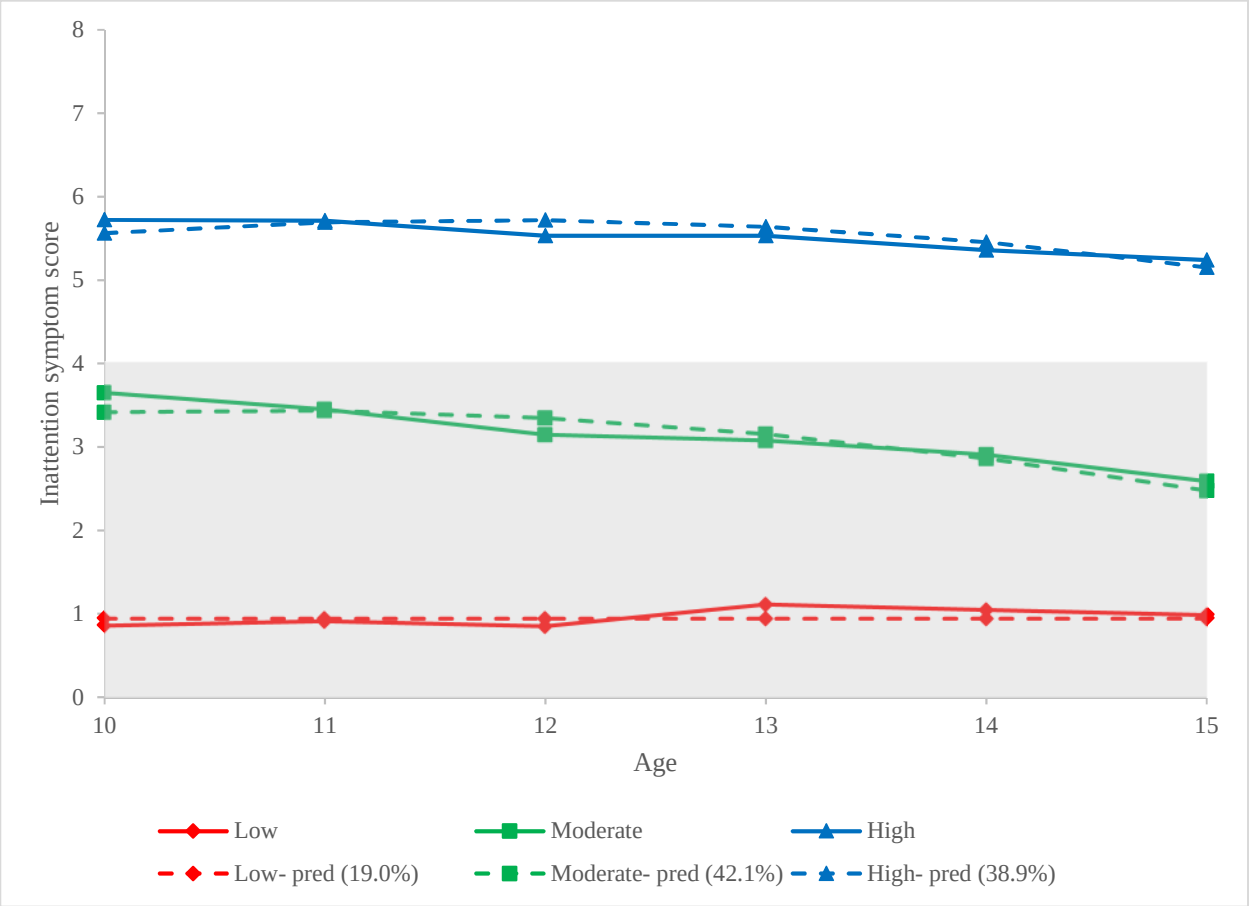
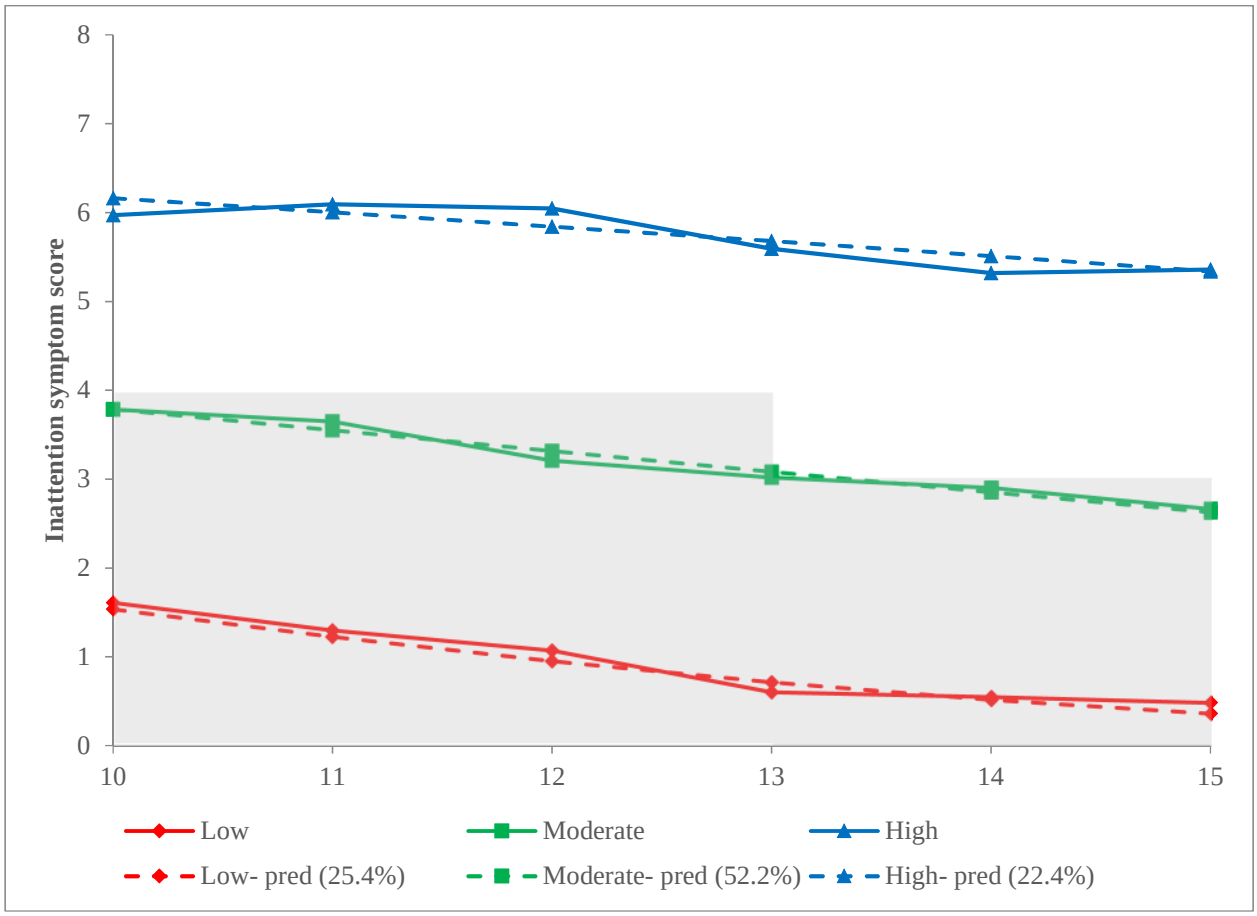


Figure 3.4b. Inattention symptom score trajectories (mother ratings) - Predicted versus observed trajectories



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CHAPTER 4

Association of hyperactivity and inattention symptom score trajectories with cigarette smoking frequency in late adolescence and daily/heavy smoking in young adulthood among boys of low socioeconomic status

ABSTRACT

Background: Although children with attention-deficit hyperactivity disorder (ADHD) have a higher risk of becoming smokers than other children, little is known about the risks associated with the trajectories of ADHD's two symptom domains--hyperactivity and inattention.

Objective: We investigated the associations of symptom score trajectories of hyperactivity and inattention from ages 10 to 15 with cigarette smoking frequency at ages 16-17 (late adolescence) and daily and heavy (one pack or more per day) cigarette smoking at ages 23 and 28 (young adulthood).

Methods: In a cohort of 1,037 kindergarten boys from low socioeconomic neighborhoods, three symptom score trajectories of hyperactivity and of inattention that differed by baseline scores (high, moderate, low) at ages 10-15 years were previously constructed. At ages 16 and 17, participants self-reported their cigarette smoking frequency and, at ages 23 and 28, their current daily and heavy smoking. We developed logistic regression models of associations between symptom trajectories and smoking outcomes in late adolescence and young adulthood, adjusting for covariates and analyzing adolescent smoking and other substance use as potential mediators.

Results: High vs. low symptom trajectories of either hyperactivity or inattention were associated with nearly doubled odds of high smoking frequency (≥40 times in the past year) in late adolescence (hyperactivity: OR=1.97 [95% CI=1.30-2.98]; inattention: OR=1.87 [1.27-2.76]). Participants in the high vs. low inattention symptom trajectory also had doubled odds of daily (OR=2.67 [1.53-4.64]) and heavy cigarette smoking (OR=1.95 [1.10-3.45]) in young adulthood. High frequency of cigarette smoking in late adolescence mediated the associations of inattention symptom trajectories with daily and heavy smoking in young adulthood, contributing to about 11-23% of the total associations.

Conclusions: In boys of low socioeconomic backgrounds, high symptom score trajectories of hyperactivity and inattention were associated with more frequent cigarette smoking in late adolescence. High inattention symptom trajectory also increased the risk of daily and heavy cigarette smoking in young adulthood, partially mediated by high frequency smoking in late adolescence. Children with high baseline levels (especially if persistent over time) of hyperactivity and/or inattention might benefit from behavioral interventions to manage symptoms and preventive interventions against cigarette smoking.

INTRODUCTION

Cigarette smoking is associated with a wide range of diseases and is the leading cause of preventable death, responsible for nearly six million deaths per year worldwide.[1] In the United States alone, cigarette smoking accounts for more than 480,000 deaths each year.[2] Smoking in adolescence is a particularly critical public health concern because individuals who start smoking in adolescence are more likely than those who start later to transition to daily and heavy smoking and to develop nicotine dependence,[3-6] increasing their risk of morbidity and mortality.[7] Although, over the past fifty years, cigarette smoking prevalence in the United States has declined substantially, in 2015, 31.1% of adolescents in the 12th grade reported ever having smoked cigarettes.[8]

Subpopulations at elevated risk of cigarette smoking in adolescence include individuals with attention-deficit hyperactivity disorder (ADHD).[4,9-13] The literature indicates that children with ADHD are more likely than those without ADHD to smoke cigarettes in adolescence and to progress from ever smoking to daily smoking in early adulthood.[4,9-13] However, the roles of component symptoms and symptom domains of ADHD are less clear.[4,11,14-19] Some studies have indicated that inattention, but not hyperactivity, is linked to smoking in adolescence and young adulthood.[20-24]

Some studies have further suggested that the risk of cigarette smoking outcomes may be dependent on symptom level and symptom persistence, such that as the number of ADHD symptoms increases, so do the risks of daily smoking and of heavy smoking in young adulthood.[25,26] Furthermore, children who continue to have ADHD in late adolescence or adulthood are more likely to report past-year smoking and daily smoking in young adulthood than individuals whose childhood ADHD has remitted.[23,27]

In the past decade, to account for symptom level and persistence of ADHD, a number of studies have used trajectory analytic methods, such as growth mixed models and latent class growth analyses (LCGA), to track the symptom courses and domains of ADHD across multiple time points.[28-39] Those approaches have revealed that, contrary to what prior persistence analyses based on two time points have suggested, symptoms wax and wane and may not follow a linear path.[27,40,41] Studies have also found considerable heterogeneity in symptom courses among different individuals within a population. For example, although hyperactivity symptoms tend to decline over time, some individuals have persistently high symptom levels.[28,34,39,42,43]

Studies of the symptom courses (or trajectories) of ADHD and its symptom domains are accumulating, but few have examined associations with smoking outcomes. Two studies have assessed the association of symptom trajectories of hyperactivity and inattention across ages 6 and 12, and nicotine abuse/dependence in young adulthood.[35,44] However, evaluations of nicotine abuse and dependence as outcomes in early adolescence or even early adulthood may be premature.[23] To date, no trajectory studies have been conducted on more age-appropriate smoking outcomes, such as cigarette smoking frequency in adolescence or daily and heavy smoking in young adulthood. In fact, frequency of cigarette smoking in late adolescence is a crucial prognostic factor for future problematic smoking behaviors in later life.[45,46] The number of days on which an adolescent smoked has been shown to predict future daily smoking and nicotine dependence in adulthood.[45,46]

Boys of low socioeconomic status (SES) represent an at-risk population for cigarette smoking.[4,22,47,48] Numerous studies have indicated that male gender and low SES are independent risk factors for cigarette smoking in adolescence.[9,49,50] However, few studies have assessed these relationships simultaneously among individuals with different levels and

persistence of ADHD symptoms. Given their inherent elevated risk of cigarette smoking, low SES boys represent an important target risk group that may benefit from public health interventions toward ADHD symptom reduction and cigarette smoking prevention and cessation programs.

This study, which utilized longitudinal data on a sample of boys from low SES areas, addresses the associations between trajectories of hyperactivity and inattention symptom scores from ages 6 to 15 and three outcomes:

1. Frequency of cigarette smoking at ages 16 and 17 (late adolescence)
2. Current daily cigarette smoking and heavy cigarette smoking at ages 23 and 28 (young adulthood)
3. Current daily cigarette smoking and heavy cigarette smoking in young adulthood, differentiating direct effects from indirect effects mediated by cigarette smoking frequency alone and in combination with frequency of alcohol use, marijuana use, and other drug use in late adolescence

METHODS

Participants

Participants were boys meeting study selection criteria (i.e., both biological parents were born in Canada and mother tongue was French) from 53 schools located in the low SES areas (with mean household SES level lower than the provincial norm) in Montreal, Canada, whose kindergarten teachers agreed to participate in the Longitudinal and Experimental Study of Low Socioeconomic Status Boys (ELEM) in 1984 when the boys were 6 years old.

Measures: Exposures

Hyperactivity and inattention symptom score trajectories

Boys were classified into three symptom score trajectories--low, moderate, and high-- for hyperactivity and inattention separately, based on their symptom scores on the hyperactivity subscale and the inattentiveness subscale of the Social Behavior Questionnaire (SBQ) between childhood (age 6 years) and mid-adolescence (age 15 years). Kindergarten teachers rated the hyperactivity and inattention of all 1,037 boys when they were age 6 years. Both teachers and mothers rated the boys' symptoms from age 10 through age 15 years annually.

The hyperactivity subscale consisted of two items: a) "restless; runs about or jumps up and down; doesn't keep still," and b) "squirmy, fidgety child." Each item was rated on a 3-point scale: "doesn't apply (0)," "sometimes applies (1)," and "certainly applies (2)." In each rating year, the teacher and mother's scores on the two items were summed to produce a total score for hyperactivity ranging from 0 to 4. The inattentiveness subscale consisted of four items: a) "has poor concentration or short attention span," b) "inattentive," c) "gives up easily," and d) "stares into space." Each item was rated on a 3-point scale: "doesn't apply (0)," "sometimes applies (1)," and "certainly applies (2)." In each rating year, teacher's and mother's scores on the four items were summed to produce a total score for inattention ranging from 0 to 8.

As described in paper 2, we constructed symptom score trajectories using LCGA. We developed two sets of symptom score trajectories each for hyperactivity and inattention based on teacher ratings (using data from ages 6 through 15 years) and mother ratings (using data from ages 10 through 15 years), separately. We then developed a number of mixture models assuming different numbers of trajectory groups and different orders for hyperactivity and inattention symptom scores individually, using the proc traj procedure in SAS, all assuming a censored normal distribution. We then selected the model that best fit the data as the final model based on

the smallest (i.e., least negative) Bayesian information criterion (BIC), and the largest probability of being the correct model (pj).

Measures: Outcomes

Cigarette smoking frequency in adolescence

The deviant and delinquent activities subsection of the Social Adaptation Questionnaire (QAS), administered to the participants at ages 16 and 17 years, asked how many times they had smoked cigarettes in the past 12 months. Response choices were "never," "1 or 2 times," "3 to 5 times," "6 to 9 times," "10 to 19 times," "20 to 39 times," and "40 or more times." Cigarette smoking frequency in late adolescence was defined as the highest frequency reported in either of the two years. For the regression analyses described later, we grouped cigarette smoking frequency into "never," "1 to 39 times," and "40 or more times," due to the bimodal distribution observed in the data; most participants in the sample either never used cigarettes or reported using cigarettes at the highest frequency.

Current daily and heavy cigarette smoking in young adulthood

At ages 23 and 28 years, participants completed the substance use subsection of the Questionnaire Sur le Developpement du Jeune Adulte (QDJA) [Questionnaire on the Development of Young Adults], which asked participants if they currently smoked cigarettes. Response choices were, "every day," "on occasion," and "never." We defined current daily smoking as a response of "every day" at either age 23 or age 28 years. Participants who reported every day or on occasion were asked how many cigarettes they smoked in the past week. We defined heavy smoking as at least 140 cigarettes in the past week, equivalent to an average of 20 cigarettes or one pack per day, at either age 23 or age 28.

Measures: Confounding and mediating variables

Confounding variables: Externalizing and internalizing behavioral problems in childhood

In addition to inattention (for the analysis of hyperactivity symptom score trajectories), and hyperactivity (for the analysis of inattention symptom score trajectories), opposition problems, and anxiety were evaluated as potential confounding variables based on teachers' ratings of subscales of the SBQ when the boys were 6 years old. The opposition subscale consisted of five items: a) "doesn't share material used for a task in the classroom," b) "irritable, quick to 'fly off the handle'," c) "is disobedient," d) "blames others," and e) "inconsiderate of others." The anxiety subscale consisted of six items: a) "is worried. Worries about many things," b) "tends to do things on his own, rather solitary," c) "appears miserable, unhappy, tearful, or distressed," d) "tends to be fearful or afraid of new things or new situations," e) "cries easily," and f) "stares into space." Each item of the subscales was rated on a 3-point scale: "doesn't apply (0)," "sometimes applies (1)," and "certainly applies (2)." Total scores were computed for each subscale, with ranges of 0-10 for opposition and 0-12 for anxiety.

Confounding variables: Family intactness, parental occupational prestige, and mother's smoking status during pregnancy

Parental and familial risk factors considered for potential confounding variables included family intactness (having two biological parents vs. single parent or others), mother's and father's occupational prestige, and mother's smoking status during pregnancy (yes/no), which were based on or derived from information provided by the mother via a questionnaire when the boys were 6 years old. Occupational prestige was defined according to the socioeconomic index developed by Blishen and colleagues.[51]

Mediating variables: Cigarette smoking frequency, frequency of alcohol use, marijuana use, and use of other drugs in late adolescence

For the analysis in which we assessed potential indirect effects of hyperactivity and inattention symptom score trajectories on current daily and heavy cigarette smoking in young adulthood, cigarette smoking frequency in late adolescence, as described above in the Outcomes section, was assessed as a mediating variable. Additional mediating variables considered included frequency of alcohol, marijuana, and other drug use (i.e., psychedelics, cocaine, amphetamines, barbiturates, tranquilizers, heroin, narcotics, and inhalants), which were based on participants' self-reported responses to questions about the number of times they had used a particular substance in the past 12 months, as part of the QAS at ages 16 and 17 years. We coded use frequency as the highest frequency reported in the two years for each substance, and dichotomized scores at the median level (i.e., alcohol: 10 or more times, marijuana: 1 or more times, other drugs: 1 or more times) based on the distribution observed in the data.

Consideration of missing data

The distributions of hyperactivity and inattention symptom scores, cigarette smoking outcomes, and potential confounding and mediating variables were assessed for outliers and missingness. Most variables had less than 10% of missing data, except for the following: mother’s (15.3%) and father’s occupational prestige (15.8%), cigarette smoking frequency in late adolescence (18.0%), daily cigarette smoking (43.2%) and heavy cigarette smoking (32.0%) in young adulthood, due to non-response or loss to follow-up.

We imputed missing values for all potential confounding and mediating variables, and cigarette smoking outcomes using the multiple imputation procedure and the fully conditional specification method. We conducted five imputations, which yielded five separate imputed datasets for modeling the association between hyperactivity and inattention symptom score trajectories and cigarette smoking outcomes in late adolescence and young adulthood. Results

generated from the five imputed datasets were combined and averaged for valid statistical inference. We did not conduct multiple imputations on the longitudinal data for hyperactivity and inattention symptom scores used to identify trajectories, because the proc traj procedure in SAS automatically used maximum likelihood estimation to account for missing values.

Multiple imputation assumes that data are missing at random (MAR), meaning that missing values should not be systematically different from observed values once observed data are taken into account. For example, if missing values on cigarette smoking frequency were higher than observed values, but only because boys with high inattention symptom scores were less likely to report their cigarette smoking frequency, adjustment of boys' inattention symptom scores would minimize bias arising from missingness. To determine the effects of a range of violations of the MAR assumption on the results of the analyses, we conducted a series of sensitivity analyses. Specifically, we planted a range of bias factors in the multiple imputation procedure, such that the imputed data were systematically inflated or deflated by a percentage from what they would have been if the data were actually MAR. We then conducted a series of sensitivity analyses using biased imputed data and identified the "tipping point" at which the results on the association between symptom trajectories and cigarette smoking outcomes were reversed from being statistically significant in the main analysis to not significant. Lastly, we assessed the plausibility of the bias factor in relation to possible nonrandom missingness.

Analysis

The distributions of participants' behavioral problem scores and parental and familial characteristics at baseline were described and compared between symptom score trajectories of hyperactivity and inattention, respectively, using chi-square tests for categorical variables and

one-way ANOVA for continuous variables. We conducted analyses for the symptom score trajectories as developed based on teacher and mother ratings, separately.

To assess the associations between hyperactivity and inattention symptom score trajectories and the various cigarette smoking outcomes in late adolescence and young adulthood, we developed both simple and multivariable ordinal (for cigarette smoking frequency) or binomial (for daily cigarette smoking and heavy cigarette smoking) logistic regression models. Potential confounding variables that were adjusted for in the multivariable analyses varied between models. They were first hypothesized based on literature and then tested using the current data based on two criteria: 1) association with the symptom score trajectories, and 2) association with the cigarette smoking outcome. We assessed Criterion 1 based on results of the analysis of baseline characteristics described above and results of the multivariable risk factor analyses in Paper 2. For Criterion 2, we conducted simple ordinal or binomial logistic regression analyses to assess the statistical significance of each of the potential confounding variables in relationship to the various cigarette smoking outcomes. Table 1 in Appendix 3 lists the confounding variables that were included in each of the logistic regression models in the study.

We assessed the frequency of cigarette smoking, alcohol use, marijuana use, and other drug use in late adolescence as potential mediators of the relationships of symptom score trajectories with daily cigarette smoking and heavy cigarette smoking in young adulthood, using the four-step procedure proposed by Baron and Kenny (see Figure 4.1).[52] First, the total association of the symptom score trajectories with the cigarette smoking outcome in young adulthood (shown as path ***c*** in the figure) was evaluated in a multivariable binomial logistic regression, adjusting for potential confounding variables. Second, the association of the symptom

score trajectories with the potential mediator (shown as path ***a*** in the figure) was assessed in a multivariable ordinal logistic regression, adjusting for potential confounding variables. Third, the association of the potential mediator with the cigarette smoking outcome (shown as path ***b*** in the figure) was evaluated using a multivariable binomial logistic regression, adjusting for symptom score trajectories and potential confounding variables. Fourth, the direct association of the symptom score trajectories with the cigarette smoking outcome (shown as path ***c'*** in the figure) was assessed using a multivariable binomial regression, adjusting for the potential mediator and potential confounding variables. We declared a potential mediator as a true mediator if it met the following three criteria: 1) most relationships assessed in the four steps (with Step 2 and 3 being the key relationships) were statistically significant at $p<0.05$; 2) Sobel test of mediation yielded a $p<0.05$; and 3) the total effect (path ***c)*** and the direct effect (path ***c'***) of the symptom score trajectories on the cigarette smoking outcomes in young adulthood were meaningfully different (operationalized in this study as a minimum 10% difference in ORs). If frequency of alcohol use, marijuana use, and other drug use were found to be independent, statistically significant mediators, we planned to assess the potential joint mediation by cigarette smoking frequency in combination with frequency of alcohol use, marijuana use and other drug use in late adolescence. In so doing, we planned to conduct a separate Sobel test with all potential mediators entered into a joint model as part of the last step of the Baron and Kenny procedure, and to assess the incremental change in the direct effect in the presence of four potential mediators combined relative to that of cigarette smoking frequency alone.

Figures 4.2a-4.2f illustrate the theoretical framework of the relationships between hyperactivity and inattention symptom score trajectories based on teacher ratings, potential

confounding variables, potential mediators, and cigarette smoking outcomes. Similar theoretical frameworks were developed for symptom score trajectories based on mother ratings (not shown).

Of note, the Baron and Kenny procedure is a traditional approach to assess mediation and is grounded on a number of assumptions, including a) no interaction between the exposure and the mediator; b) no unmeasured confounding between exposure and the outcome; c) no unmeasured confounding between the mediator and the outcome; d) no unmeasured confounding between the exposure and the mediator; and e) no confounding between the mediator and the outcome is caused by the exposure.[53-57]

With regard to assumption a, we tested this assumption by conducting a sensitivity analysis for Step 4 of the Baron and Kenny procedure for each of the mediation analyses by including an interaction term between the exposure (symptom score trajectories) and the mediator (i.e., smoking frequency in late adolescence). None of the interaction terms reached statistical significance. Nevertheless, when we compared the analyses with versus without the exposure-mediator interaction term, we observed an appreciable change (more than 10%) in the OR estimates for the association of symptom score trajectories with smoking outcomes in young adulthood, suggesting that some amount of exposure-mediator interaction may be present.

With regard to assumption b, just as in any observational study, result inference regarding the overall association between an exposure and outcome is only valid if all exposure-outcome confounding is fully controlled. Yet, because unmeasured confounding, by nature, is unobserved, one can only adjust for observed confounding and assume that any residual confounding is minimal. This also holds true in the context of mediation analysis, where confounding control is extended to the relationship of the mediator with the exposure and the outcome (assumptions c-e). For our mediation analyses, we adjusted for observed exposure-outcome, exposure-mediator,

and mediator-outcome confounding as depicted in Figures 4.2b-c and Figures 4.2e-f, and summarized in Table 1 in Appendix 3. According to these theoretical frameworks, none of the symptom score trajectories causes any of the observed confounding between the mediator (i.e., smoking frequency in late adolescence) and cigarette smoking outcomes. As such, assumption f is reasonable.

RESULTS

Hyperactivity and inattention symptom trajectories

As paper 2 describes, at baseline, teachers provided ratings for hyperactivity and inattention symptoms on nearly all 1,037 boys. At age 10 years, 973-977 (93.8%-94.2%) of the boys had teacher ratings, and 701-702 (67.6%-67.7%) had mother ratings; between ages 11 and 15 years, 753-942 (72.6%-90.8%) had teacher ratings and 621-731 (59.9%-70.5%) had mother ratings. Across all age years, 536-712 (51.7%-68.7%) of the boys had both informants' ratings.

Hyperactivity symptom scores were found to follow a declining trend between childhood and mid-adolescence, whereas inattention symptom scores stayed relatively stable. For each symptom domain, the study participants followed one of three trajectories – low, moderate, or high – based on their symptom scores. Based on teacher ratings, of the 1,037 participants in the sample, 196 (18.9%) followed the high declining hyperactivity symptom score trajectory, and 403 (38.8%) followed the high inattention symptom score trajectory. Based on mother ratings, 149 (14.4%) of the participants fell into the high hyperactivity symptom score trajectory, and 202 (19.5%) fell into the high inattention symptom score trajectory.

Baseline characteristics

Tables 4.1a and 4.1b present participants' externalizing and internalizing behavioral problems and parental and familial characteristics measured at age 6 years in the overall sample

and stratified by hyperactivity symptom score trajectories based on teacher ratings and mother ratings. On average, boys presented with a baseline behavioral symptom score that is less than 3 for hyperactivity, inattention, and opposition, and anxiety. These baseline symptom scores translate to having about one to two symptoms of hyperactivity, inattention, and opposition, and anxiety at baseline. The majority of participants (74.7%) came from an intact family and had parents with moderate occupational prestige. Boys in the high hyperactivity symptom score trajectory had higher symptom scores for baseline hyperactivity, inattention, and opposition, and were more likely to come from a non-intact family (all $p<0.05$) and to have anxious parents than boys in the other trajectories.

Tables 4.1c and 4.1d present distributions of the same baseline characteristics of the overall sample, and stratified by inattention symptom score trajectories based on teacher and mother ratings. Similar increased symptom scores for baseline hyperactivity, inattention, and opposition were observed among participants in the high inattention symptom score trajectory. Boys in the high trajectory were also more likely to come from non-intact families; their mothers were younger, and their parents' occupational prestige was lower than boys with lower scores.

Frequency of cigarette smoking and other substance use in late adolescence

Table 4.2a and Table 4.2b present data on the frequency of cigarette smoking and use of alcohol, marijuana, and other drugs in late adolescence and current daily and heavy cigarette smoking in young adulthood overall and by hyperactivity symptom score trajectories based on teachers' (Table 4.2a) and mothers' (Table 4.2b) ratings. Table 4.2c and Table 4.3d present data on the same behaviors by inattention symptom score trajectories based on teachers' (Table 4.2c) and mothers' (Table 4.2d) ratings.

Frequency of cigarette smoking

The frequency of cigarette smoking in late adolescence had a bimodal distribution. Almost half of the participants (48.5%) had never smoked cigarettes, but 36.1% had smoked 40 or more times in the past year; the remaining 15.4% of participants had smoked 1-39 times in the past year). Smoking frequency also had a bimodal distribution within the various hyperactivity and inattention symptom score trajectory groups. A greater proportion of participants in the high symptom score trajectory groups (according to both teachers' and mothers' ratings) reported having smoked 40 or more times than in the other trajectory groups ($p<0.05$).

Frequency of alcohol, marijuana, and other drug use

Most participants (84.0%) had used alcohol in the past year, and 46.1% had done so 10 or more times, but use frequency did not differ by hyperactivity or inattention symptom trajectory. Approximately 47.8% of participants had never used marijuana; 11.3% had used it once or twice, and 17.6% had used it 40 or more times in the past year. Participants in the moderate and high trajectories for hyperactivity and inattention symptoms were more likely to have used marijuana than the low trajectory group based on teachers' ratings but not mothers' ratings.

The use of other drugs was considerably less common. About one-third of the sample (28.5%) reported having used other drugs at least once, and the proportion of users was higher in the high trajectory groups for both hyperactivity and inattention symptoms than in the other groups, again based on teachers' ratings but not mothers' ratings.

Current daily and heavy cigarette smoking in young adulthood

Table 4.2a and Table 4.2b present data from the young adult questionnaires on current daily and heavy cigarette smoking by hyperactivity symptom score trajectories based on teachers' and mothers' ratings. Table 4.2c and Table 4.2d present the data by inattention symptom score trajectories based on teachers' and mothers' ratings.

Daily cigarette smoking

Nearly 70% of young adults in the high symptom score trajectory group vs. approximately 40% in the low symptom score trajectory group for both hyperactivity and inattention had smoked daily in the past week ($p<0.001$).

Heavy cigarette smoking

Nearly 30% of young adults in both the high hyperactivity symptom score trajectory and the high inattention symptom score trajectory reported smoking at least 140 cigarettes in the past week, compared to less than 20% of those in the low hyperactivity and low inattention trajectories ($p<0.05$).

Association between symptom score trajectories and frequency of cigarette smoking in late adolescence

Hyperactivity symptom score trajectories

Table 4.3a presents the crude and adjusted ORs for the association of hyperactivity symptom score trajectory based on teacher ratings with frequent cigarette smoking in late adolescence. Compared to (late) adolescents in the low symptom score trajectory group, those in the high symptom score trajectory group had twice the odds of having smoked cigarettes 40 or more times in the past year ($p<0.001$). This association remained statistically significant after adjustment for oppositional behavior and mother's smoking during pregnancy (adjusted OR=1.97, 95% confidence interval [CI]=1.30-2.98, p=0.002). In addition, those in the moderate symptom score trajectory group had >60% higher odds of having smoked cigarettes 40 or more times in the past year than those in the low trajectory group (adjusted OR=1.61, 95% CI=1.21-2.14, p=0.001).

Although, based on mother ratings, adolescents in the high hyperactivity symptom score trajectory also were more likely than others to have smoked frequently in the past year (crude OR=1.44, 95% CI=1.01-2.05, p=0.045), the adjusted OR was not statistically significant (see Table 4.3b).

Inattention symptom score trajectories

Table 4.3c presents the crude and adjusted ORs for the association of inattention symptom score trajectory based on teachers' ratings with frequent cigarette smoking in late adolescence. Participants in the high symptom score trajectory group had approximately 1.44 times the odds of frequent smoking compared to participants in the low symptom trajectory group (95% CI=1.21-1.71, p<0.001)--an association that was strengthened after adjustment for hyperactivity and opposition (OR=1.87, 95% CI=1.27-2.76, p=0.002).

The association of frequent smoking with inattention symptom score trajectory based on mothers' ratings was similar (see Table 4.3d). The crude and adjusted ORs were 1.84 (95% CI=1.27-2.66, p=0.001) and 1.75 (95% CI=1.20-2.54, p=0.003), respectively.

Association of symptom score trajectories with current daily and heavy cigarette smoking in young adulthood

Hyperactivity symptom score trajectories

Table 4.4a and Table 4.5a present the crude and adjusted odds ratios (OR) for the associations of hyperactivity symptom score trajectory based on teacher ratings with current daily cigarette smoking and current heavy cigarette smoking in young adulthood. The crude OR for current daily smoking among young adults in the high (vs. low) hyperactivity symptom trajectory group was 2.42 (95% CI=1.56-3.76, p<0.001); and the crude OR for current heavy cigarette smoking among young adults in the high (vs. low) hyperactivity symptom trajectory

group was 2.65 (95% CI=1.47-4.78, p=0.002). The associations with moderate trajectory were weaker but also positive. However, after adjustment, none of the associations was statistically significant.

The crude ORs were weaker when hyperactivity symptom score trajectories were based on mother ratings, and none of the adjusted ORs was statistically significant (Table 4.4b and Table 4.5b).

Inattention symptom score trajectories

Table 4.4c and Table 4.5c present the crude and adjusted ORs for the associations of current daily cigarette smoking and current heavy cigarette smoking in young adulthood with inattention symptom score trajectories based on teacher ratings. The crude OR for current daily smoking among young adults in the high (vs. low) inattention symptom score trajectory was 3.13 (95% CI=1.99-4.94, p<0.001); the crude OR for current heavy cigarette smoking among young adults in the high (vs. low) inattention symptom score trajectory was 2.65 (95% CI=1.53-4.60, p<0.001) . After adjustment for confounding variables, these associations remained statistically significant (current daily cigarette smoking: OR=2.67, 95% CI=1.53-4.64, p=0.001; current heavy cigarette smoking: OR=1.95, 95% CI=1.10-3.45, p=0.022). The crude ORs for the associations of both current daily and current heavy smoking with moderate inattention trajectory were weaker and, with adjustment, not statistically significant.

As Tables 4.4d and 4.5d show, the ORs for the associations of daily and heavy smoking with high inattention trajectory based on mother ratings were slightly weaker overall; the adjusted OR for daily smoking remained statistically significant (OR=2.53, 95% CI=1.53-4.18, p<0.001).

Mediation analysis of frequency of cigarette smoking alone and in combination with frequency of alcohol use, marijuana use, and other drug use in late adolescence

To address the possible associations of certain behaviors in late adolescence with smoking in young adulthood, as well as with the symptom score trajectories observed in childhood, we undertook mediation analyses. Because the above analyses indicated that hyperactivity symptom score trajectory was not associated with smoking outcomes in young adulthood, we did not analyze mediation of those associations.

Association between inattention symptom score trajectories and daily cigarette smoking in young adulthood

Table 4.6a (panel 1) presents results of the analysis of cigarette smoking frequency in late adolescence as a potential mediator of the association between inattention symptom score trajectories, based on teacher ratings, and daily cigarette smoking in young adulthood. Odds ratios and 95% CIs obtained from the assessments of the four-step procedure proposed by Baron and Kenny are shown.

Cigarette smoking frequency in late adolescence mediated the association of interest based on data from the four steps of the Baron and Kenny procedure. Specifically, Step 1 confirmed the overall association of high inattention symptom score trajectory and current daily cigarette smoking in young adulthood (OR=2.67, p=0.001). Step 2 showed an association between high inattention symptom score trajectory and cigarette smoking frequency in late adolescence (OR=1.87, p=0.002). Step 3 showed a strong association between cigarette smoking frequency in late adolescence and current daily cigarette smoking in young adulthood (OR=13.99, p<0.001), upon adjustment for inattention symptom score trajectories. Step 4 showed an independent association of high symptom score trajectory and current daily cigarette

smoking in young adulthood (OR=2.23, p=0.011). The Sobel test statistic for mediation confirmed that cigarette smoking frequency in late adolescence mediated that association (Z=3.04, p=0.002). After adjustment for cigarette smoking frequency in late adolescence, the association between high inattention symptom score trajectory and current daily cigarette smoking was attenuated by 17%.

We also evaluated frequency of alcohol use, marijuana use, and other drug use during late adolescence using the four steps of the Barron and Kenny procedure (Table 4.6a, panels 2-4). None of those behaviors met all criteria for mediation. We did not conduct a joint mediation analysis of cigarette smoking frequency in combination with frequency of the other substances.

Mediation analyses conducted on the inattention symptom score trajectories based on mother ratings yielded results similar to those based on teacher ratings as shown above (Table 4.6b). Again, cigarette smoking frequency in late adolescence met all four Baron and Kenny's criteria. Based on Sobel's test statistic, cigarette smoking frequency in late adolescence mediated the association between high inattention symptom score trajectory and current daily cigarette smoking in young adulthood (Z=2.85, p=0.004). After adjustment for cigarette smoking frequency, the association was attenuated by 11%.

Association between inattention symptom score trajectories and current heavy cigarette smoking in young adulthood

Table 4.7a (panel 1) presents results of the analysis of frequency of cigarette smoking in late adolescence as a potential mediator of the association between inattention symptom score trajectories based on teacher ratings and current heavy cigarette smoking in young adulthood. Cigarette smoking frequency met the four Barron and Kenny criteria (steps). Specifically, Step 1 confirmed the overall association of high inattention symptom score trajectory associated with

current heavy cigarette smoking in young adulthood (OR=1.95, p=0.022). Step 2 showed the association between high inattention symptom score trajectory and cigarette smoking frequency in late adolescence (OR=1.87, p=0.002). Step 3 showed the association between cigarette smoking frequency in late adolescence and current heavy cigarette smoking in young adulthood (OR=5.92, p<0.001), after adjustment for the inattention symptom score trajectories. Step 4 showed the independent association of high symptom score trajectory and current heavy cigarette smoking in young adulthood, which was no longer statistically significant (OR=1.50, p=0.248). The Sobel test statistic for mediation indicated that cigarette smoking frequency in late adolescence was a statistically significant mediator (Z=2.90, p=0.004). After adjustment for cigarette smoking frequency in late adolescence, the association between high inattention symptom score trajectory and current heavy smoking was attenuated by 23%.

We conducted similar analyses of alcohol use, marijuana use, and other drug use during late adolescence (Table 4.7a, panels 2-4). None of those behaviors met all criteria for mediation. We did not conduct a joint mediation analysis of cigarette smoking frequency in combination with frequency of the other substances.

The results of mediation analyses based on mothers' inattention symptom score trajectories were similar to those based on teacher ratings (Table 4.7b). They met all Baron and Kenny's criteria. Sobel's test statistics were Z=2.85 (p=0.004) for current daily smoking and Z=2.68 (p=0.007) for current heavy cigarette smoking. The association was attenuated by 22% after adjustment for cigarette smoking frequency.

Sensitivity analyses: assessment of violations of the MAR assumption

Because the three cigarette smoking outcome measures in this study had considerable missing data (cigarette smoking frequency 18.0%; daily cigarette smoking 43.2%; heavy

cigarette smoking 32.9%) and were multiply imputed, we conducted tipping point sensitivity analyses to assess the effects of a range of violations of the MAR assumption on our study findings. Specifically, we planted a number of bias factors in the multiple imputation procedure for the smoking outcome measures, and assessed their effects on the main findings. Table 2a in Appendix 3 illustrates the sensitivity analysis for the association between hyperactivity symptom score trajectories, based on teacher ratings, and cigarette smoking frequency in late adolescence. We inflated the imputed values of the log odds of high cigarette smoking frequency by a range of factors (0.51 to 1.18); bias factors beyond these two values were implausible and would have made the proportions of individuals across the three categories of cigarette frequency total more than 100%. Within that range, the main findings remained statistically significant, implying that only an implausibly large violation of MAR in the cigarette smoking frequency imputation would have more than minimal effects on our conclusion.

We conducted similar tipping point sensitivity analyses for daily cigarette smoking and heavy cigarette smoking (Table 2b and Table 2c in Appendix 3). For daily cigarette smoking, at two tipping points (0.76 and 1.10), the statistically nonsignificant main findings would have been reversed. These findings suggest that if participants who did not provide daily cigarette smoking data--whether due to non-response or loss to follow-up--were (2.14 to 3.00 times) more likely to have smoked daily than the participants with data, then the association between high hyperactivity symptom score trajectory and daily cigarette smoking would have been statistically significant. It is plausible that some daily smokers may have refused to answer this question, potentially due to shame. However, because the QDJA was a self-reported questionnaire rather than an interviewer-administered survey, participants' incentive to impress or shield their shame should have been minimized. Research has generally shown that self-reports of cigarette

smoking are valid.[58,59] In addition, it is implausible that daily smokers would have much less ability or incentive than others to stay engaged in the study follow-up. Hence, we believe that violations of MAR would have minimal effects on our findings.

Likewise, for heavy cigarette smoking, at two tipping points (0.64 and 1.16), the non-statistically significant main findings were reversed. For similar reasons, we believe that the impact of a violation of MAR would be minimal.

We conducted similar tipping point analyses to assess the impact of potential violations of MAR on inattention symptom score trajectories based on teacher ratings, as shown in Tables 3a-3c in Appendix 3. Tipping points were not reached for cigarette smoking frequency, and were of great magnitudes for daily and heavy cigarette smoking. We therefore expect the impact of violations of MAR to have been minimal.

DISCUSSION

The current study assessed the frequency of cigarette smoking in late adolescence and daily and heavy cigarette smoking in young adulthood across different symptom score trajectories of hyperactivity and inattention symptoms in childhood through mid-adolescence in a sample of low SES boys. We found that high (vs. low) symptom score trajectories in both domains were associated with frequent cigarette smoking in late adolescence. High symptom score trajectory for inattention, but not for hyperactivity, was also associated with daily and heavy cigarette smoking in young adulthood. Through mediation analyses, we observed that part of the association with daily cigarette smoking and with heavy cigarette smoking in young adulthood was attributable to high cigarette frequency in late adolescence. In other words, boys in the high inattention symptom score trajectory group were more likely to smoke cigarettes at

high frequency in late adolescence than those in the low trajectory, thereby increasing their risk for subsequent daily and heavy cigarette smoking as young adults.

Unlike some past studies, which suggested that inattention, but not hyperactivity, was associated with cigarette smoking in adolescence,[20-24] we found that boys in either of the high symptom score trajectory groups had nearly twice the odds of becoming frequent smokers in late adolescence, compared to boys in the low symptom score trajectory groups. Perhaps for boys with high hyperactivity symptom scores, engaging in high frequency of cigarette smoking was a product of amplified behavioral disinhibition or lack of self-control.[26,60,61] As for boys with high inattention symptom scores, smoking may have been self-medication with nicotine for their attention deficits.[62-65]

However, high symptom score trajectory of inattention and not hyperactivity was indeed associated with daily and heavy cigarette smoking in young adulthood. As the overall shapes of hyperactivity and inattention symptom score trajectories in Paper 2 show, hyperactivity symptoms tended to dissipate over time, whereas inattention symptoms generally remained stable. If smoking behavior associated with hyperactivity was indeed due to behavioral disinhibition, then as hyperactivity symptoms declined over time, the impulse to engage in high levels of smoking would also dissipate. As for inattention, because symptoms tended to stay stable as boys grew up, the need for stimulation from nicotine would remain high among boys with high symptom scores.

Our finding that high cigarette smoking frequency in late adolescence mediated the relationship between inattention and current and heavy smoking in young adulthood is consistent with the current understanding that cigarette smoking in adolescence is a risk factor for future problematic smoking outcomes in adulthood.[3-6] Unlike past studies, which largely focused on the

role of smoking initiation or lifetime smoking in adolescence, we analyzed frequency of cigarette smoking in late adolescence as a prognostic factor of daily and heavy cigarette smoking in young adulthood, highlighting the role of adolescence as a sensitive developmental period with potentially profound implications for adult life.[3-6]

We found that approximately 11-17% of the total association of inattention symptom score trajectories with daily cigarette smoking, and 22-23% of that association with heavy smoking in young adulthood, was attributable to cigarette smoking frequency in late adolescence. Because adjustment did not completely attenuate those associations, we concluded that cigarette smoking frequency in late adolescence was a partial and not a complete mediator. Among boys who never smoked in late adolescence, those in the high inattention symptom score trajectory group had 2.23-2.25 times higher odds of daily cigarette smoking and 1.26-1.50 times higher odds of heavy smoking as young adults than those in the low inattention symptom score trajectory group. In other words, high inattention symptom scores independently conferred elevated risks for problematic cigarette smoking behaviors well beyond late adolescence.

We also evaluated use of alcohol, marijuana, and other drugs in late adolescence as potential mediators of the association of inattention symptom score trajectories with daily and heavy cigarette smoking in young adulthood; none of those behaviors met the criteria for mediation.

According to the gateway theory, substance users start experimenting with tobacco or alcohol use in adolescence and proceed to use more addictive substances, such as marijuana, psychoactive and illicit drugs, in adulthood.[66-68] In other words, cigarette smoking generally precedes other substance use. It is therefore not surprising that we did not find use of other substances in late adolescence to predict daily and heavy cigarette smoking in young adulthood.

For all study analyses, we evaluated symptom score trajectories that were derived based on two informants' ratings--teachers' and mothers'--separately. These analyses yielded largely similar results regarding associations with cigarette smoking outcomes in late adolescence and young adulthood. This consistency in findings confirms that both teachers' and mothers' reports are informative sources, consistent with the literature; some clinicians and researchers regard data from both sources as necessary for the full characterization of symptoms score trajectories.[69,70] The consistency of the two sources, given their different perspectives and settings, also serves to validate our findings.

Our results, nonetheless, have limitations. First, because the QAS offers choices of ranges of cigarette smoking frequency, we could not analyze cigarette smoking as a continuous (integer) variable, determine the full range of use among study participants, or analyze monthly or daily use. In particular, the highest frequency level offered was 40 or more times in the past year without an upper limit.

Second, all cigarette smoking outcomes were based on participants' self-report and were subject to misclassification. The distinction between the two lowest categories of smoking frequency (1 or 2 times vs. 3 to 5 times) may have been too small for participants to appreciate and may have contributed to the low prevalence of those levels. We therefore grouped all frequency responses between "never" and "40 or more times" into one category in all analyses to enhance interpretability and statistical power.

Third, the focus of the current study was on cigarette smoking outcomes in late adolescence and young adulthood. We did not evaluate frequencies of alcohol use, marijuana use, and drug use in late adolescence and subsequent progression to more problematic use in young adulthood as endpoints. Although substance use is a critical public health problem,

especially among individuals with ADHD, the assessment of the full range of substances as outcomes was beyond the scope of our study.

Fourth, the prevalence of missing data in the cigarette smoking variables ranged from 18.0% for cigarette smoking frequency in late adolescence to 43.2% for daily cigarette smoking. To avoid possible bias due to using only complete data for our analyses, we imputed missing values using the multiple imputation procedure and the fully conditional specification method. We further conducted sensitivity analyses to verify that our models were robust and at low risk for violation of the MAR assumption.

Fifth, the study sample was limited to boys from low SES and francophone neighborhoods in Montreal. Although this population was chosen to illustrate the relationship between hyperactivity and inattention symptoms and smoking behaviors in adolescence and young adulthood in a high-risk population, the generalizability of our findings to girls and to children of other ethnic backgrounds or higher SES may be limited. However, our study participants were recruited from a large sampling pool of 52 schools in low SES neighborhoods in Montreal, and the response rate of eligible teachers to participate in the study when it first started in 1984 was high at 87%. We therefore believe that selection bias was minimal and the sample reasonably representative of the target population.

Sixth, we adopted the Baron and Kenny procedure to assess potential mediation between symptom score trajectories and cigarette smoking outcomes in young adulthood. As discussed above, one of the assumptions of this (traditional) mediation approach is no interaction between the exposure and the mediator. Because we observed an appreciable change in the OR estimates for the association of symptom score trajectories with smoking outcomes in young adulthood before and after adjusting for the exposure-mediator interaction term, it is possible that some

amount of exposure-mediator interaction may be present. If true, the direct effect estimates presented in this study may be biased. Relatedly, other assumptions of the Baron and Kenny procedure include no unmeasured confounding between exposure and outcome, mediator and outcome, and exposure and mediator, all of which cannot be tested. While we controlled for observed confounding in our analyses, residual confounding was inevitable. In the event that unmeasured confounding did exist, the direct effect estimates from the mediation analyses presented in this study may be biased.

We note that the Baron and Kenny procedure is a simplistic approach to evaluate mediation, and causal inference methods may provide more sophisticated approaches and are more robust to account for the presence of exposure-mediator interaction. Our analyses based on this traditional approach, nevertheless, serve to provide an overview of the mediation pathway between symptom score trajectories and smoking outcomes in young adulthood--a research topic that has been largely unexplored to date. Importantly, our study underscores the presence of mediation between inattention symptom score trajectories and daily and heavy cigarette smoking in young adulthood. As a next step, we intend to apply a causal mediation approach to further assess the mediation pathways discussed in this study. Such approach will allow for more precise estimates of the direct effects and indirect effects, the latter of which were not assessed in this study.

Despite its limitations, this study may substantially enhance our understanding of the symptom score trajectories of hyperactivity and inattention, and their relationships with cigarette smoking behaviors in late adolescence and young adulthood. Prior trajectory studies have evaluated the relationship of symptom scores with nicotine abuse or dependence, but none has assessed more age-appropriate cigarette smoking outcomes in late adolescence and young

adulthood as we did in this study. This study is one of the first to document associations of high hyperactivity and inattention symptom score trajectories with frequent cigarette smoking in adolescence and with daily and heavy cigarette smoking in young adulthood, as well as the mediating role of frequent cigarette smoking in late adolescence among individuals with high inattention symptom scores.

In light of these findings, high symptom score trajectories of inattention and hyperactivity may be important targets for smoking prevention and cessation efforts. Not only do they increase the risk of frequent smoking in late adolescence, they also increase the risk of transition to daily and heavy cigarette smoking in young adulthood. Public health smoking prevention and cessation program developers should consider targeting individuals with histories of as well as high and persistent levels of hyperactivity and inattention symptoms. Individuals with elevated inattention symptom scores over time may represent an especially high-risk group. Perhaps behavioral interventions to manage hyperactivity and inattention symptoms might help to prevent or reduce smoking in adolescence and later life.

Table 4.1a. Participants' baseline behavioral symptoms and parental characteristics, overall and by hyperactivity symptom trajectories based on teacher ratings

	Total sample N= 1037	Low trajectory N= 325	Moderate trajectory N= 516	High trajectory N= 196	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	0.45 ± 0.85 [0.00]	1.48 ± 1.36 [1.00]	2.76 ± 1.33 [3.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	1.90 ± 2.05 [1.00]	2.76 ± 2.34 [2.00]	3.72 ± 2.29 [4.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	1.17 ± 1.67 [0.00]	2.68 ± 2.48 [2.00]	4.27 ± 2.97 [4.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.99 ± 2.72 [3.00]	2.96 ± 2.62 [2.00]	2.80 ± 2.43 [2.00]	0.900
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	26.11 ± 4.49 [25.70]	25.13 ± 4.68 [24.56]	24.27 ± 4.64 [23.84]	<0.001*
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.80 ± 5.46 [28.24]	28.42 ± 5.44 [27.67]	27.26 ± 6.06 [26.06]	<0.001*
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	40.49 ± 12.47 [40.42]	38.05 ± 12.22 [37.10]	34.96 ± 10.18 [29.98]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	42.05 ± 14.07 [38.35]	38.97 ± 12.44 [35.31]	36.02 ± 10.63 [32.57]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	320 (98.5%)	488 (94.6%)	192 (98%)	
Intact	747 (74.7%)	261 (81.6%)	362 (74.2%)	124 (64.6%)	<0.001*
Not intact	253 (25.3%)	59 (18.4%)	126 (25.8%)	68 (35.4%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	243 (74.8%)	355 (68.8%)	121 (61.7%)	
Yes	186 (25.9%)	55 (22.6%)	96 (27%)	35 (28.9%)	0.338
No	533 (74.1%)	188 (77.4%)	259 (73%)	86 (71.1%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	217 (66.8%)	309 (59.9%)	105 (53.6%)	
Yes	112 (17.7%)	26 (12%)	61 (19.7%)	25 (23.8%)	0.015*
No	519 (82.3%)	191 (88%)	248 (80.3%)	80 (76.2%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	136 (41.8%)	227 (44%)	71 (36.2%)	
Yes	168 (38.7%)	48 (35.3%)	86 (37.9%)	34 (47.9%)	0.196
No	266 (61.3%)	88 (64.7%)	141 (62.1%)	37 (52.1%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 4.1b. Participants' baseline behavioral symptoms and parental characteristics, overall and by hyperactivity symptom trajectories based on mother ratings

	Total sample N= 1037	Low trajectory N= 547	Moderate trajectory N= 341	High trajectory N= 149	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	1.45 ± 1.45 [1.00]	1.02 ± 1.31 [0.00]	2.10 ± 1.50 [2.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	2.70 ± 2.36 [2.00]	2.23 ± 2.16 [2.00]	3.56 ± 2.33 [3.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	2.54 ± 2.60 [2.00]	1.99 ± 2.29 [1.00]	3.58 ± 2.91 [3.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.90 ± 2.56 [2.00]	2.90 ± 2.62 [2.00]	3.19 ± 2.80 [3.00]	0.568
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	25.17 ± 4.64 [24.74]	25.65 ± 4.74 [25.33]	24.78 ± 4.46 [24.07]	0.078
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.51 ± 5.34 [27.82]	28.18 ± 5.63 [27.56]	28.09 ± 6.29 [27.30]	0.285
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	37.06 ± 11.92 [33.32]	40.66 ± 12.12 [40.42]	37.01 ± 11.96 [34.17]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	38.22 ± 11.79 [34.44]	41.98 ± 14.11 [37.67]	37.71 ± 12.55 [34.45]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	513 (93.8%)	341 (100%)	146 (98%)	
Intact	747 (74.7%)	374 (72.9%)	273 (80.1%)	100 (68.5%)	0.011*
Not intact	253 (25.3%)	139 (27.1%)	68 (19.9%)	46 (31.5%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	342 (62.5%)	260 (76.2%)	117 (78.5%)	
Yes	186 (25.9%)	85 (24.9%)	62 (23.8%)	39 (33.3%)	0.126
No	533 (74.1%)	257 (75.1%)	198 (76.2%)	78 (66.7%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	302 (55.2%)	228 (66.9%)	101 (67.8%)	
Yes	112 (17.7%)	49 (16.2%)	34 (14.9%)	29 (28.7%)	0.007*
No	519 (82.3%)	253 (83.8%)	194 (85.1%)	72 (71.3%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	209 (38.2%)	156 (45.7%)	69 (46.3%)	
Yes	168 (38.7%)	90 (43.1%)	48 (30.8%)	30 (43.5%)	0.039*
No	266 (61.3%)	119 (56.9%)	108 (69.2%)	39 (56.5%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 4.1c. Participants' baseline behavioral symptoms and parental characteristics, overall and by inattention symptom trajectories based on teacher ratings

	Total sample N= 1037	Low trajectory N= 191	Moderate trajectory N= 443	High trajectory N= 403	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	0.63 ± 1.04 [0.00]	1.25 ± 1.36 [1.00]	1.93 ± 1.53 [2.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	1.03 ± 1.40 [0.00]	2.29 ± 2.00 [2.00]	3.88 ± 2.39 [4.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	1.18 ± 1.65 [0.00]	2.40 ± 2.52 [2.00]	3.26 ± 2.78 [3.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.25 ± 2.32 [2.00]	2.89 ± 2.65 [2.00]	3.33 ± 2.64 [3.00]	<0.001*
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	26.34 ± 4.66 [25.82]	25.45 ± 4.63 [25.05]	24.56 ± 4.58 [24.15]	<0.001*
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.79 ± 5.13 [28.37]	28.54 ± 5.69 [27.72]	27.86 ± 5.67 [27.25]	0.032*
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	42.92 ± 13.09 [43.80]	38.37 ± 11.81 [38.35]	35.68 ± 11.11 [30.11]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	44.30 ± 15.13 [41.22]	39.66 ± 12.90 [35.47]	36.51 ± 10.42 [33.60]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	188 (98.4%)	427 (96.4%)	385 (95.5%)	
Intact	747 (74.7%)	160 (85.1%)	323 (75.6%)	264 (68.6%)	<0.001*
Not intact	253 (25.3%)	28 (14.9%)	104 (24.4%)	121 (31.4%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	145 (75.9%)	319 (72%)	255 (63.3%)	
Yes	186 (25.9%)	34 (23.4%)	78 (24.5%)	74 (29%)	0.350
No	533 (74.1%)	111 (76.6%)	241 (75.5%)	181 (71%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	125 (65.4%)	280 (63.2%)	226 (56.1%)	
Yes	112 (17.7%)	15 (12%)	48 (17.1%)	49 (21.7%)	0.071
No	519 (82.3%)	110 (88%)	232 (82.9%)	177 (78.3%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	81 (42.4%)	203 (45.8%)	150 (37.2%)	
Yes	168 (38.7%)	23 (28.4%)	80 (39.4%)	65 (43.3%)	0.081
No	266 (61.3%)	58 (71.6%)	123 (60.6%)	85 (56.7%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 4.1d. Participants' baseline behavioral symptoms and parental characteristics, overall and by inattention symptom trajectories based on mother ratings

	Total sample N= 1037	Low trajectory N= 228	Moderate trajectory N= 607	High trajectory N= 202	P-value[1]
Participants' behavioral symptoms	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	**mean ± SD [median]**	
Hyperactivity[2]	1.40 ± 1.45 [1.00]	0.96 ± 1.28 [0.00]	1.47 ± 1.47 [1.00]	1.70 ± 1.49 [2.00]	<0.001*
Inattention[3]	2.67 ± 2.33 [2.00]	1.77 ± 1.94 [1.00]	2.74 ± 2.33 [2.00]	3.49 ± 2.41 [3.00]	<0.001*
Opposition[4]	2.51 ± 2.60 [2.00]	1.76 ± 2.17 [1.00]	2.68 ± 2.70 [2.00]	2.84 ± 2.56 [2.00]	<0.001*
Anxiety[5]	2.94 ± 2.62 [2.00]	2.75 ± 2.61 [2.00]	2.96 ± 2.63 [2.00]	3.10 ± 2.58 [3.00]	0.233
Parents' demographic characteristics					
Mother's age (years) at birth of participant	25.28 ± 4.66 [24.83]	26.39 ± 4.94 [26.01]	24.98 ± 4.58 [24.60]	24.89 ± 4.36 [24.44]	<0.001*
Father's age (years) at birth of participant	28.33 ± 5.58 [27.62]	28.74 ± 5.77 [28.05]	28.30 ± 5.37 [27.46]	27.94 ± 5.92 [27.30]	0.221
Mother's occupational prestige[6]	38.29 ± 12.10 [38.28]	42.07 ± 12.84 [43.59]	36.82 ± 11.67 [32.51]	38.16 ± 11.59 [38.32]	<0.001*
Father's occupational prestige[6]	39.44 ± 12.86 [35.15]	43.08 ± 14.38 [39.10]	38.40 ± 12.14 [34.84]	37.99 ± 12.14 [33.30]	<0.001*
Family structure[7]	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	1000 (96.4%)	227 (99.6%)	575 (94.7%)	198 (98%)	
Intact	747 (74.7%)	184 (81.1%)	420 (73%)	143 (72.2%)	0.042*
Not intact	253 (25.3%)	43 (18.9%)	155 (27%)	55 (27.8%)	
Parent's mental health					
Parent's depression[8]					
No. (%) of participants with data	719 (69.3%)	182 (79.8%)	389 (64.1%)	148 (73.3%)	
Yes	186 (25.9%)	37 (20.3%)	92 (23.7%)	57 (38.5%)	<0.001*
No	533 (74.1%)	145 (79.7%)	297 (76.3%)	91 (61.5%)	
Parent's anxiety[8]					
No. (%) of participants with data	631 (60.8%)	159 (69.7%)	338 (55.7%)	134 (66.3%)	
Yes	112 (17.7%)	16 (10.1%)	57 (16.9%)	39 (29.1%)	<0.001*
No	519 (82.3%)	143 (89.9%)	281 (83.1%)	95 (70.9%)	
Mother's smoking during pregnancy					
Cigarettes					
No. (%) of participants with data	434 (41.9%)	106 (46.5%)	234 (38.6%)	94 (46.5%)	
Yes	168 (38.7%)	33 (31.1%)	101 (43.2%)	34 (36.2%)	0.092
No	266 (61.3%)	73 (68.9%)	133 (56.8%)	60 (63.8%)	

[1] P-value was derived from chi-square for categorical variables and wilcoxon rank-sum test for continuous variables.
[2] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.
[3] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.
[4] Opposition was assessed by teachers when participants were aged 6 using the opposition subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 10.
[5] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.
[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.
[7] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.
[8] Parents' depression and anxiety were based on parents' self report when participants were 6. Having at least one parent with depression and anxiety constituted a yes response.

Table 4.2a. Substance use outcomes in late adolescence and young adulthood by hyperactivity symptom trajectories based on teacher ratings

	Total sample N= 1037	Low trajectory N= 325	Moderate trajectory N= 516	High trajectory N= 196	P-value[1]
Substance use frequency in late adolescence					
Cigarettes					
Past-year use frequency	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	850 (82%)	274 (84.3%)	428 (82.9%)	148 (75.5%)	
Never	412 (48.5%)	158 (57.7%)	194 (45.3%)	60 (40.5%)	0.031*
1 or 2 times	56 (6.6%)	16 (5.8%)	32 (7.5%)	8 (5.4%)	
3 to 5 times	24 (2.8%)	9 (3.3%)	11 (2.6%)	4 (2.7%)	
6 to 9 times	16 (1.9%)	5 (1.8%)	6 (1.4%)	5 (3.4%)	
10 to 19 times	22 (2.6%)	9 (3.3%)	10 (2.3%)	3 (2%)	
20 to 39 times	13 (1.5%)	3 (1.1%)	7 (1.6%)	3 (2%)	
40 or more times	307 (36.1%)	74 (27%)	168 (39.3%)	65 (43.9%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	274 (84.3%)	428 (82.9%)	148 (75.5%)	
Never	412 (48.5%)	158 (57.7%)	194 (45.3%)	60 (40.5%)	0.002*
1 to 39 times	131 (15.4%)	42 (15.3%)	66 (15.4%)	23 (15.5%)	
40 or more times	307 (36.1%)	74 (27%)	168 (39.3%)	65 (43.9%)	
Alcohol					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	274 (84.3%)	428 (82.9%)	148 (75.5%)	
Never	136 (16%)	53 (19.3%)	61 (14.3%)	22 (14.9%)	0.251
1 or 2 times	120 (14.1%)	35 (12.8%)	65 (15.2%)	20 (13.5%)	
3 to 5 times	102 (12%)	25 (9.1%)	55 (12.9%)	22 (14.9%)	
6 to 9 times	100 (11.8%)	33 (12%)	56 (13.1%)	11 (7.4%)	
10 to 19 times	146 (17.2%)	51 (18.6%)	63 (14.7%)	32 (21.6%)	
20 to 39 times	116 (13.6%)	40 (14.6%)	59 (13.8%)	17 (11.5%)	
40 or more times	130 (15.3%)	37 (13.5%)	69 (16.1%)	24 (16.2%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	274 (84.3%)	428 (82.9%)	148 (75.5%)	
Never to 9 times	458 (53.9%)	146 (53.3%)	237 (55.4%)	75 (50.7%)	0.596
10 or more times	392 (46.1%)	128 (46.7%)	191 (44.6%)	73 (49.3%)	

Marijuana					
Past-year use frequency					
No. (%) of participants with data	849 (81.9%)	274 (84.3%)	428 (82.9%)	147 (75%)	
Never	406 (47.8%)	149 (54.4%)	189 (44.2%)	68 (46.3%)	0.002*
1 or 2 times	96 (11.3%)	30 (10.9%)	53 (12.4%)	13 (8.8%)	
3 to 5 times	48 (5.7%)	12 (4.4%)	28 (6.5%)	8 (5.4%)	
6 to 9 times	45 (5.3%)	16 (5.8%)	26 (6.1%)	3 (2%)	
10 to 19 times	56 (6.6%)	18 (6.6%)	30 (7%)	8 (5.4%)	
20 to 39 times	49 (5.8%)	21 (7.7%)	22 (5.1%)	6 (4.1%)	
40 or more times	149 (17.6%)	28 (10.2%)	80 (18.7%)	41 (27.9%)	
Past-year use frequency recategorized					
No. (%) of participants with data	849 (81.9%)	274 (84.3%)	428 (82.9%)	147 (75%)	
Never	406 (47.8%)	149 (54.4%)	189 (44.2%)	68 (46.3%)	0.028*
1 or more times	443 (52.2%)	125 (45.6%)	239 (55.8%)	79 (53.7%)	
Other drugs					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	274 (84.3%)	428 (82.9%)	148 (75.5%)	
Never	608 (71.5%)	211 (77%)	305 (71.3%)	92 (62.2%)	0.009*
1 or 2 times	75 (8.8%)	24 (8.8%)	35 (8.2%)	16 (10.8%)	
3 to 5 times	41 (4.8%)	16 (5.8%)	15 (3.5%)	10 (6.8%)	
6 to 9 times	28 (3.3%)	7 (2.6%)	15 (3.5%)	6 (4.1%)	
10 to 19 times	38 (4.5%)	8 (2.9%)	20 (4.7%)	10 (6.8%)	
20 to 39 times	23 (2.7%)	4 (1.5%)	17 (4%)	2 (1.4%)	
40+ times	37 (4.4%)	4 (1.5%)	21 (4.9%)	12 (8.1%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	274 (84.3%)	428 (82.9%)	148 (75.5%)	
Never	608 (71.5%)	211 (77%)	305 (71.3%)	92 (62.2%)	0.005*
1 or more times	242 (28.5%)	63 (23%)	123 (28.7%)	56 (37.8%)	
Cigarette smoking frequency in young adulthood					
Current daily use					
No. (%) of participants with data	589 (56.8%)	193 (59.4%)	286 (55.4%)	110 (56.1%)	
Yes	320 (54.3%)	86 (44.6%)	159 (55.6%)	75 (68.2%)	<0.001*
No	269 (45.7%)	107 (55.4%)	127 (44.4%)	35 (31.8%)	
Heavy use					
No. (%) of participants with data	696 (67.1%)	228 (70.2%)	339 (65.7%)	129 (65.8%)	
Yes	138 (19.8%)	29 (12.7%)	72 (21.2%)	37 (28.7%)	<0.001*
No	558 (80.2%)	199 (87.3%)	267 (78.8%)	92 (71.3%)	
[1] P-value was derived from chi-square tests.					

Table 4.2b. Substance use outcomes in late adolescence and young adulthood by hyperactivity symptom trajectories based on mother ratings

	Total sample N= 1037	Low trajectory N= 547	Moderate trajectory N= 341	High trajectory N= 149	P-value[1]
Substance use frequency in late adolescence					
Cigarettes					
Past-year use frequency	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	850 (82%)	419 (76.6%)	298 (87.4%)	133 (89.3%)	
Never	412 (48.5%)	212 (50.6%)	146 (49%)	54 (40.6%)	0.086
1 or 2 times	56 (6.6%)	26 (6.2%)	22 (7.4%)	8 (6%)	
3 to 5 times	24 (2.8%)	7 (1.7%)	9 (3%)	8 (6%)	
6 to 9 times	16 (1.9%)	7 (1.7%)	7 (2.3%)	2 (1.5%)	
10 to 19 times	22 (2.6%)	9 (2.1%)	12 (4%)	1 (0.8%)	
20 to 39 times	13 (1.5%)	6 (1.4%)	6 (2%)	1 (0.8%)	
40 or more times	307 (36.1%)	152 (36.3%)	96 (32.2%)	59 (44.4%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	419 (76.6%)	298 (87.4%)	133 (89.3%)	
Never	412 (48.5%)	212 (50.6%)	146 (49%)	54 (40.6%)	0.050*
1 to 39 times	131 (15.4%)	55 (13.1%)	56 (18.8%)	20 (15%)	
40 or more times	307 (36.1%)	152 (36.3%)	96 (32.2%)	59 (44.4%)	
Alcohol					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	419 (76.6%)	298 (87.4%)	133 (89.3%)	
Never	136 (16%)	64 (15.3%)	46 (15.4%)	26 (19.5%)	0.683
1 or 2 times	120 (14.1%)	58 (13.8%)	42 (14.1%)	20 (15%)	
3 to 5 times	102 (12%)	54 (12.9%)	36 (12.1%)	12 (9%)	
6 to 9 times	100 (11.8%)	51 (12.2%)	39 (13.1%)	10 (7.5%)	
10 to 19 times	146 (17.2%)	78 (18.6%)	47 (15.8%)	21 (15.8%)	
20 to 39 times	116 (13.6%)	52 (12.4%)	46 (15.4%)	18 (13.5%)	
40 or more times	130 (15.3%)	62 (14.8%)	42 (14.1%)	26 (19.5%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	419 (76.6%)	298 (87.4%)	133 (89.3%)	
Never to 9 times	458 (53.9%)	227 (54.2%)	163 (54.7%)	68 (51.1%)	0.779
10 or more times	392 (46.1%)	192 (45.8%)	135 (45.3%)	65 (48.9%)	

Marijuana					
Past-year use frequency					
No. (%) of participants with data	849 (81.9%)	419 (76.6%)	297 (87.1%)	133 (89.3%)	
Never	406 (47.8%)	211 (50.4%)	137 (46.1%)	58 (43.6%)	0.464
1 or 2 times	96 (11.3%)	50 (11.9%)	29 (9.8%)	17 (12.8%)	
3 to 5 times	48 (5.7%)	27 (6.4%)	16 (5.4%)	5 (3.8%)	
6 to 9 times	45 (5.3%)	17 (4.1%)	21 (7.1%)	7 (5.3%)	
10 to 19 times	56 (6.6%)	23 (5.5%)	23 (7.7%)	10 (7.5%)	
20 to 39 times	49 (5.8%)	19 (4.5%)	22 (7.4%)	8 (6%)	
40 or more times	149 (17.6%)	72 (17.2%)	49 (16.5%)	28 (21.1%)	
Past-year use frequency recategorized					
No. (%) of participants with data	849 (81.9%)	419 (76.6%)	297 (87.1%)	133 (89.3%)	
Never	406 (47.8%)	211 (50.4%)	137 (46.1%)	58 (43.6%)	0.306
1 or more times	443 (52.2%)	208 (49.6%)	160 (53.9%)	75 (56.4%)	
Other drugs					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	419 (76.6%)	298 (87.4%)	133 (89.3%)	
Never	608 (71.5%)	302 (72.1%)	213 (71.5%)	93 (69.9%)	0.370
1 or 2 times	75 (8.8%)	35 (8.4%)	30 (10.1%)	10 (7.5%)	
3 to 5 times	41 (4.8%)	19 (4.5%)	17 (5.7%)	5 (3.8%)	
6 to 9 times	28 (3.3%)	14 (3.3%)	7 (2.3%)	7 (5.3%)	
10 to 19 times	38 (4.5%)	22 (5.3%)	10 (3.4%)	6 (4.5%)	
20 to 39 times	23 (2.7%)	9 (2.1%)	12 (4%)	2 (1.5%)	
40+ times	37 (4.4%)	18 (4.3%)	9 (3%)	10 (7.5%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	419 (76.6%)	298 (87.4%)	133 (89.3%)	
Never	608 (71.5%)	302 (72.1%)	213 (71.5%)	93 (69.9%)	0.891
1 or more times	242 (28.5%)	117 (27.9%)	85 (28.5%)	40 (30.1%)	
Cigarette smoking frequency in young adulthood					
Current daily use					
No. (%) of participants with data	589 (56.8%)	295 (53.9%)	199 (58.4%)	95 (63.8%)	
Yes	320 (54.3%)	166 (56.3%)	89 (44.7%)	65 (68.4%)	<0.001*
No	269 (45.7%)	129 (43.7%)	110 (55.3%)	30 (31.6%)	
Heavy use					
No. (%) of participants with data	696 (67.1%)	349 (63.8%)	239 (70.1%)	108 (72.5%)	
Yes	138 (19.8%)	73 (20.9%)	32 (13.4%)	33 (30.6%)	<0.001*
No	558 (80.2%)	276 (79.1%)	207 (86.6%)	75 (69.4%)	

[1] P-value was derived from chi-square tests.

Table 4.2c. Substance use outcomes in late adolescence and young adulthood by inattention symptom trajectories based on teacher ratings

	Total sample N= 1037	Low trajectory N= 191	Moderate trajectory N= 443	High trajectory N= 403	P-value[1]
Substance use frequency in late adolescence					
Cigarettes					
Past-year use frequency	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	850 (82%)	166 (86.9%)	365 (82.4%)	319 (79.2%)	
Never	412 (48.5%)	94 (56.6%)	178 (48.8%)	140 (43.9%)	<0.001*
1 or 2 times	56 (6.6%)	12 (7.2%)	35 (9.6%)	9 (2.8%)	
3 to 5 times	24 (2.8%)	10 (6%)	7 (1.9%)	7 (2.2%)	
6 to 9 times	16 (1.9%)	3 (1.8%)	9 (2.5%)	4 (1.3%)	
10 to 19 times	22 (2.6%)	8 (4.8%)	9 (2.5%)	5 (1.6%)	
20 to 39 times	13 (1.5%)	1 (0.6%)	8 (2.2%)	4 (1.3%)	
40 or more times	307 (36.1%)	38 (22.9%)	119 (32.6%)	150 (47%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	166 (86.9%)	365 (82.4%)	319 (79.2%)	
Never	412 (48.5%)	94 (56.6%)	178 (48.8%)	140 (43.9%)	<0.001*
1 to 39 times	131 (15.4%)	34 (20.5%)	68 (18.6%)	29 (9.1%)	
40 or more times	307 (36.1%)	38 (22.9%)	119 (32.6%)	150 (47%)	
Alcohol					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	166 (86.9%)	365 (82.4%)	319 (79.2%)	
Never	136 (16%)	27 (16.3%)	51 (14%)	58 (18.2%)	0.219
1 or 2 times	120 (14.1%)	19 (11.4%)	51 (14%)	50 (15.7%)	
3 to 5 times	102 (12%)	20 (12%)	40 (11%)	42 (13.2%)	
6 to 9 times	100 (11.8%)	24 (14.5%)	40 (11%)	36 (11.3%)	
10 to 19 times	146 (17.2%)	37 (22.3%)	63 (17.3%)	46 (14.4%)	
20 to 39 times	116 (13.6%)	22 (13.3%)	58 (15.9%)	36 (11.3%)	
40 or more times	130 (15.3%)	17 (10.2%)	62 (17%)	51 (16%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	166 (86.9%)	365 (82.4%)	319 (79.2%)	
Never to 9 times	458 (53.9%)	90 (54.2%)	182 (49.9%)	186 (58.3%)	0.087
10 or more times	392 (46.1%)	76 (45.8%)	183 (50.1%)	133 (41.7%)	

Marijuana					
Past-year use frequency					
No. (%) of participants with data	849 (81.9%)	166 (86.9%)	364 (82.2%)	319 (79.2%)	
Never	406 (47.8%)	99 (59.6%)	168 (46.2%)	139 (43.6%)	0.006*
1 or 2 times	96 (11.3%)	16 (9.6%)	41 (11.3%)	39 (12.2%)	
3 to 5 times	48 (5.7%)	12 (7.2%)	18 (4.9%)	18 (5.6%)	
6 to 9 times	45 (5.3%)	10 (6%)	18 (4.9%)	17 (5.3%)	
10 to 19 times	56 (6.6%)	10 (6%)	30 (8.2%)	16 (5%)	
20 to 39 times	49 (5.8%)	9 (5.4%)	21 (5.8%)	19 (6%)	
40 or more times	149 (17.6%)	10 (6%)	68 (18.7%)	71 (22.3%)	
Past-year use frequency recategorized					
No. (%) of participants with data	849 (81.9%)	166 (86.9%)	364 (82.2%)	319 (79.2%)	
Never	406 (47.8%)	99 (59.6%)	168 (46.2%)	139 (43.6%)	0.002*
1 or more times	443 (52.2%)	67 (40.4%)	196 (53.8%)	180 (56.4%)	
Other drugs					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	166 (86.9%)	365 (82.4%)	319 (79.2%)	
Never	608 (71.5%)	143 (86.1%)	256 (70.1%)	209 (65.5%)	<0.001*
1 or 2 times	75 (8.8%)	6 (3.6%)	39 (10.7%)	30 (9.4%)	
3 to 5 times	41 (4.8%)	9 (5.4%)	14 (3.8%)	18 (5.6%)	
6 to 9 times	28 (3.3%)	4 (2.4%)	11 (3%)	13 (4.1%)	
10 to 19 times	38 (4.5%)	3 (1.8%)	20 (5.5%)	15 (4.7%)	
20 to 39 times	23 (2.7%)	1 (0.6%)	9 (2.5%)	13 (4.1%)	
40+ times	37 (4.4%)	0 (0%)	16 (4.4%)	21 (6.6%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	166 (86.9%)	365 (82.4%)	319 (79.2%)	
Never	608 (71.5%)	143 (86.1%)	256 (70.1%)	209 (65.5%)	<0.001*
1 or more times	242 (28.5%)	23 (13.9%)	109 (29.9%)	110 (34.5%)	
Cigarette smoking frequency in young adulthood					
Current daily use					
No. (%) of participants with data	589 (56.8%)	125 (65.4%)	269 (60.7%)	195 (48.4%)	
Yes	320 (54.3%)	48 (38.4%)	136 (50.6%)	136 (69.7%)	<0.001*
No	269 (45.7%)	77 (61.6%)	133 (49.4%)	59 (30.3%)	
Heavy use					
No. (%) of participants with data	696 (67.1%)	146 (76.4%)	322 (72.7%)	228 (56.6%)	
Yes	138 (19.8%)	18 (12.3%)	60 (18.6%)	60 (26.3%)	0.003*
No	558 (80.2%)	128 (87.7%)	262 (81.4%)	168 (73.7%)	

[1] P-value was derived from chi-square tests.

Table 4.2d. Substance use outcomes in late adolescence and young adulthood by inattention symptom trajectories based on mother ratings

	Total sample N= 1037	Low trajectory N= 228	Moderate trajectory N= 607	High trajectory N= 202	P-value[1]
Substance use frequency in late adolescence					
Cigarettes					
Past-year use frequency	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
No. (%) of participants with data	850 (82%)	203 (89%)	473 (77.9%)	174 (86.1%)	
Never	412 (48.5%)	112 (55.2%)	227 (48%)	73 (42%)	0.070
1 or 2 times	56 (6.6%)	16 (7.9%)	30 (6.3%)	10 (5.7%)	
3 to 5 times	24 (2.8%)	7 (3.4%)	9 (1.9%)	8 (4.6%)	
6 to 9 times	16 (1.9%)	5 (2.5%)	9 (1.9%)	2 (1.1%)	
10 to 19 times	22 (2.6%)	8 (3.9%)	11 (2.3%)	3 (1.7%)	
20 to 39 times	13 (1.5%)	3 (1.5%)	7 (1.5%)	3 (1.7%)	
40 or more times	307 (36.1%)	52 (25.6%)	180 (38.1%)	75 (43.1%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	203 (89%)	473 (77.9%)	174 (86.1%)	
Never	412 (48.5%)	112 (55.2%)	227 (48%)	73 (42%)	0.005*
1 to 39 times	131 (15.4%)	39 (19.2%)	66 (14%)	26 (14.9%)	
40 or more times	307 (36.1%)	52 (25.6%)	180 (38.1%)	75 (43.1%)	
Alcohol					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	203 (89%)	473 (77.9%)	174 (86.1%)	
Never	136 (16%)	32 (15.8%)	71 (15%)	33 (19%)	0.763
1 or 2 times	120 (14.1%)	30 (14.8%)	70 (14.8%)	20 (11.5%)	
3 to 5 times	102 (12%)	24 (11.8%)	55 (11.6%)	23 (13.2%)	
6 to 9 times	100 (11.8%)	25 (12.3%)	61 (12.9%)	14 (8%)	
10 to 19 times	146 (17.2%)	34 (16.7%)	84 (17.8%)	28 (16.1%)	
20 to 39 times	116 (13.6%)	32 (15.8%)	58 (12.3%)	26 (14.9%)	
40 or more times	130 (15.3%)	26 (12.8%)	74 (15.6%)	30 (17.2%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	203 (89%)	473 (77.9%)	174 (86.1%)	
Never to 9 times	458 (53.9%)	111 (54.7%)	257 (54.3%)	90 (51.7%)	0.812
10 or more times	392 (46.1%)	92 (45.3%)	216 (45.7%)	84 (48.3%)	

Marijuana					
Past-year use frequency					
No. (%) of participants with data	849 (81.9%)	202 (88.6%)	473 (77.9%)	174 (86.1%)	
Never	406 (47.8%)	106 (52.5%)	220 (46.5%)	80 (46%)	0.130
1 or 2 times	96 (11.3%)	16 (7.9%)	63 (13.3%)	17 (9.8%)	
3 to 5 times	48 (5.7%)	13 (6.4%)	30 (6.3%)	5 (2.9%)	
6 to 9 times	45 (5.3%)	13 (6.4%)	20 (4.2%)	12 (6.9%)	
10 to 19 times	56 (6.6%)	18 (8.9%)	27 (5.7%)	11 (6.3%)	
20 to 39 times	49 (5.8%)	9 (4.5%)	29 (6.1%)	11 (6.3%)	
40 or more times	149 (17.6%)	27 (13.4%)	84 (17.8%)	38 (21.8%)	
Past-year use frequency recategorized					
No. (%) of participants with data	849 (81.9%)	202 (88.6%)	473 (77.9%)	174 (86.1%)	
Never	406 (47.8%)	106 (52.5%)	220 (46.5%)	80 (46%)	0.314
1 or more times	443 (52.2%)	96 (47.5%)	253 (53.5%)	94 (54%)	
Other drugs					
Past-year use frequency					
No. (%) of participants with data	850 (82%)	203 (89%)	473 (77.9%)	174 (86.1%)	
Never	608 (71.5%)	154 (75.9%)	333 (70.4%)	121 (69.5%)	0.236
1 or 2 times	75 (8.8%)	15 (7.4%)	48 (10.1%)	12 (6.9%)	
3 to 5 times	41 (4.8%)	15 (7.4%)	18 (3.8%)	8 (4.6%)	
6 to 9 times	28 (3.3%)	4 (2%)	15 (3.2%)	9 (5.2%)	
10 to 19 times	38 (4.5%)	7 (3.4%)	23 (4.9%)	8 (4.6%)	
20 to 39 times	23 (2.7%)	4 (2%)	14 (3%)	5 (2.9%)	
40+ times	37 (4.4%)	4 (2%)	22 (4.7%)	11 (6.3%)	
Past-year use frequency recategorized					
No. (%) of participants with data	850 (82%)	203 (89%)	473 (77.9%)	174 (86.1%)	
Never	608 (71.5%)	154 (75.9%)	333 (70.4%)	121 (69.5%)	0.286
1 or more times	242 (28.5%)	49 (24.1%)	140 (29.6%)	53 (30.5%)	
Cigarette smoking frequency in young adulthood					
Current daily use					
No. (%) of participants with data	589 (56.8%)	138 (60.5%)	334 (55%)	117 (57.9%)	
Yes	320 (54.3%)	55 (39.9%)	186 (55.7%)	79 (67.5%)	<0.001*
No	269 (45.7%)	83 (60.1%)	148 (44.3%)	38 (32.5%)	
Heavy use					
No. (%) of participants with data	696 (67.1%)	170 (74.6%)	397 (65.4%)	129 (63.9%)	
Yes	138 (19.8%)	23 (13.5%)	80 (20.2%)	35 (27.1%)	0.014*
No	558 (80.2%)	147 (86.5%)	317 (79.8%)	94 (72.9%)	

[1] P-value was derived from chi-square tests.

Table 4.3a. Association between hyperactivity symptom score trajectory (teacher ratings) and frequency of cigarette smoking in late adolescence

	Cigarette smoking frequency[1]					
Hyperactivity symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	2.01	(1.42,2.87)	<0.001*	1.97	(1.3,2.98)	0.002*
Moderate trajectory	1.64	(1.25,2.16)	<0.001*	1.61	(1.21,2.14)	0.001*
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Opposition[4]	-	-	-	1.02	(0.97,1.08)	0.447
Mother's smoking during pregnancy	-	-	-	0.68	(0.52,0.9)	0.007*

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Frequency of cigarette smoking was based on participants' self-reported response to the question on the number of times they had used cigarettes in the past 12 months at ages 16 and 17, as part of the Social Adaptation Questionnaire (QAS). Low to moderate frequency refers to "1 or 2 times," "3 to 5 times," "6 to 9 times," "10 to 19 times," or "20 to 39 times." High frequency refers to "40 or more times." The reference group is "never." The highest level of frequency across the two years assessed was used to define the use frequency of cigarette smoking in late adolescence.

[2] Odds ratios were derived from ordinal logistic regressions, which modeled the higher frequencies over lower ones.

[3] Hyperactivity symptom trajectories were constructed using latent class growth analysis. Hyperactivity symptoms were based on teacher ratings on the hyperactivity subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 6 to 15. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

[4] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

Table 4.3b. Association between hyperactivity symptom score trajectory (mother ratings) and frequency of cigarette smoking in late adolescence

	Cigarette smoking frequency[1]					
Hyperactivity symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	1.44	(1.01,2.05)	0.045*	1.37	(0.96,1.97)	0.084
Moderate trajectory	0.97	(0.74,1.25)	0.791	0.99	(0.77,1.29)	0.968
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Opposition[4]	-	-	-	1.05	(0.99,1.11)	0.080

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Frequency of cigarette smoking was based on participants' self-reported response to the question on the number of times they had used cigarettes in the past 12 months at ages 16 and 17, as part of the Social Adaptation Questionnaire (QAS). Low to moderate frequency refers to "1 or 2 times," "3 to 5 times," "6 to 9 times," "10 to 19 times," or "20 to 39

[2] Odds ratios were derived from ordinal logistic regressions, which modeled the higher frequencies over lower ones.

[3] Hyperactivity symptom trajectories were constructed using latent class growth analysis. Hyperactivity symptoms were based on mother ratings on the hyperactivity subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 6 to 15. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

[4] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

Table 4.3c. Association between inattention symptom score trajectory (teacher ratings) and frequency of cigarette smoking in late adolescence

	Cigarette smoking frequency[1]					
Inattention symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	1.44	(1.21,1.71)	<0.001*	1.87	(1.27,2.76)	0.002*
Moderate trajectory	0.99	(0.84,1.18)	0.921	1.34	(0.92,1.94)	0.122
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Hyperactivity[4]				1.01	(0.9,1.14)	0.818
Opposition[5]	-	-	-	1.04	(0.97,1.11)	0.262

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Frequency of cigarette smoking was based on participants' self-reported response to the question on the number of times they had used cigarettes in the past 12 months at ages 16 and 17, as part of the Social Adaptation Questionnaire (QAS). Low to moderate frequency refers to "1 or 2 times," "3 to 5 times," "6 to 9 times," "10 to 19 times," or "20 to 39 times." High frequency refers to "40 or more times." The reference group is "never." The highest level of frequency across the two years assessed was used to define the use frequency of cigarette smoking in late adolescence.

[2] Odds ratios were derived from ordinal logistic regressions, which modeled the higher frequencies over lower ones.

[3] Inattention symptom trajectories were constructed using latent class growth analysis. Inattention symptoms were based on teacher ratings on the inattentiveness subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 6 to 15. A total score was generated based on four items on the subscale for each assessed year, ranging from 0 to 8.

[4] Hyperactivity symptom scores were based on teacher ratings on the hyperactivity subscale of the SBQ when participants were age 6. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

[5] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

Table 4.3d. Association between inattention symptom score trajectory (mother ratings) and frequency of cigarette smoking in late adolescence

	Cigarette smoking frequency[1]					
Inattention symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	1.84	(1.27,2.66)	0.001*	1.75	(1.2,2.54)	0.003*
Moderate trajectory	1.45	(1.07,1.97)	0.015*	1.40	(1.03,1.91)	0.030*
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Hyperactivity[4]				1.07	(0.98,1.16)	0.119

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Frequency of cigarette smoking was based on participants' self-reported response to the question on the number of times they had used cigarettes in the past 12 months at ages 16 and 17, as part of the Social Adaptation Questionnaire (QAS). Low to moderate frequency refers to "1 or 2 times," "3 to 5 times," "6 to 9 times," "10 to 19 times," or "20 to 39

[2] Odds ratios were derived from ordinal logistic regressions, which modeled the higher frequencies over lower ones.

[3] Inattention symptom trajectories were constructed using latent class growth analysis. Inattention symptoms were based on mother ratings on the inattentiveness subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 10 to 15. A total score was generated based on four items on the subscale for each assessed year, ranging from 0 to 8.

[4] Hyperactivity symptom scores were based on teacher ratings on the hyperactivity subscale of the SBQ when participants were age 6. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

Table 4.4a. Association between hyperactivity symptom score trajectory (teacher ratings) and daily cigarette smoking in young adulthood

	Daily cigarette smoking[1]					
Hyperactivity symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	2.42	(1.56,3.76)	<0.001*	1.64	(0.87,3.08)	0.119
Moderate trajectory	1.59	(1.09,2.32)	0.017*	1.33	(0.89,1.98)	0.156
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Inattention[4]	-	-	-	1.13	(0.99,1.29)	0.073
Opposition[5]	-	-	-	1.03	(0.96,1.11)	0.384
Anxiety[6]	-	-	-	0.91	(0.83,1.01)	0.069
Father's occupational prestige[7]	-	-	-	0.99	(0.98,1.01)	0.367
Family intactness[8]	-	-	-	0.76	(0.5,1.18)	0.208

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Daily cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked if they currently smoked cigarettes. Response choices were, "everyday," "on occasion," and "never." Daily cigarette smoking refers to "everyday."

[2] Odds ratios were derived from binomial logistic regressions.

[3] Hyperactivity symptom trajectories were constructed using latent class growth analysis. Hyperactivity symptoms were based on teacher ratings on the hyperactivity subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 6 to 15. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

[4] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.

[5] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

[6] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.

[7] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

[8] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.

Table 4.4b. Association between hyperactivity symptom score trajectory (mother ratings) and daily cigarette smoking in young adulthood

	Daily cigarette smoking[1]					
Hyperactivity symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	1.63	(1.08,2.47)	0.021*	1.46	(0.96,2.22)	0.075
Moderate trajectory	0.75	(0.53,1.04)	0.085	0.79	(0.57,1.1)	0.164
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Inattention[4]				1.10	(0.99,1.22)	0.066
Opposition[5]	-	-	-	1.04	(0.95,1.14)	0.419

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Daily cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked if they currently smoked cigarettes. Response choices were, "everyday," "on occasion," and "never." Daily cigarette smoking refers to "everyday."

[2] Odds ratios were derived from binomial logistic regressions.

[3] Hyperactivity symptom trajectories were constructed using latent class growth analysis. Hyperactivity symptoms were based on mother ratings on the hyperactivity subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 10 to 15. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

[4] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.

[5] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

Table 4.4c. Association between inattention symptom score trajectory (teacher ratings) and daily cigarette smoking in young adulthood

	Daily cigarette smoking[1]					
Inattention symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	3.13	(1.99,4.94)	<0.001*	2.67	(1.53,4.64)	0.001*
Moderate trajectory	1.70	(1.12,2.6)	0.015*	1.56	(0.95,2.54)	0.074
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Hyperactivity[4]				1.07	(0.91,1.27)	0.388
Opposition[5]	-	-	-	1.04	(0.95,1.14)	0.402
Anxiety[6]	-	-	-	0.93	(0.87,0.99)	0.025*
Father's occupational prestige[7]				0.99	(0.98,1.01)	0.298
Family intactness[8]	-	-	-	0.80	(0.53,1.2)	0.270

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Daily cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked if they currently smoked cigarettes. Response choices were, "everyday," "on occasion," and "never." Daily cigarette smoking refers to "everyday."

[2] Odds ratios were derived from binomial logistic regressions.

[3] Inattention symptom trajectories were constructed using latent class growth analysis. Inattention symptoms were based on teacher ratings on the inattentiveness subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 6 to 15. A total score was generated based on four items on the subscale for each assessed year, ranging from 0 to 8.

[4] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.

[5] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

[6] Anxiety was assessed by teachers when participants were aged 6 using the anxiety subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 12.

[7] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

[8] Family structure was assessed for intactness based on parents' self report when participants were 6. "Intact" was defined as having two biological parents or having other family structures, including having a step parent, having a guardian, etc. "Not intact" was defined as having only one parent.

Table 4.4d. Association between inattention symptom score trajectory (mother ratings) and daily cigarette smoking in young adulthood

	Daily cigarette smoking[1]					
Inattention symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	2.80	(1.63,4.79)	<0.001*	2.53	(1.53,4.18)	<0.001*
Moderate trajectory	1.84	(1.14,2.99)	0.017*	1.72	(1.09,2.69)	0.021*
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Hyperactivity[4]				1.17	(0.99,1.37)	0.061

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Daily cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked if they currently smoked cigarettes. Response choices were, "everyday," "on occasion," and "never." Daily cigarette smoking refers to "everyday."

[2] Odds ratios were derived from binomial logistic regressions.

[3] Inattention symptom trajectories were constructed using latent class growth analysis. Inattention symptoms were based on mother ratings on the inattentiveness subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 10 to 15. A total score was generated based on four items on the subscale for each assessed year, ranging from 0 to 8.

[4] Hyperactivity was assessed by teachers when participants were aged 6 using the hyperactivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.

Table 4.5a. Association between hyperactivity symptom score trajectory (teacher ratings) and heavy cigarette smoking in young adulthood

	Heavy cigarette smoking[1]					
Hyperactivity symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	2.65	(1.47,4.78)	0.002*	1.90	(0.91,3.95)	0.082
Moderate trajectory	1.75	(1.02,3)	0.044*	1.47	(0.79,2.74)	0.206
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Inattention[4]	-	-	-	1.05	(0.97,1.13)	0.273
Opposition[5]	-	-	-	1.09	(1.01,1.17)	0.021*
Father's occupational prestige[6]	-	-	-	1.00	(0.98,1.02)	0.775
Mother's smoking during pregnancy	-	-	-	0.84	(0.5,1.43)	0.498

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Heavy cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked the number of cigarettes smoked in the past week. Heavy cigarette smoking was defined as 140 cigarettes (about one pack) or more.

[2] Odds ratios were derived from binomial logistic regressions.

[3] Hyperactivity symptom trajectories were constructed using latent class growth analysis. Hyperactivity symptoms were based on teacher ratings on the hyperactivity subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 6 to 15. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

[4] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.

[5] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

Table 4.5b. Association between hyperactivity symptom score trajectory (mother ratings) and heavy cigarette smoking in young adulthood

	Heavy cigarette smoking[1]					
Hyperactivity symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	1.67	(1.09,2.57)	0.019*	1.47	(0.95,2.28)	0.085
Moderate trajectory	0.72	(0.46,1.14)	0.159	0.78	(0.5,1.22)	0.264
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Inattention[4]	-	-	-	1.03	(0.93,1.14)	0.574
Opposition[5]	-	-	-	1.11	(1.04,1.2)	0.003*

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Heavy cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked the number of cigarettes smoked in the past week. Heavy cigarette smoking was defined as 140 cigarettes (about one pack) or more.

[2] Odds ratios were derived from binomial logistic regressions.

[3] Hyperactivity symptom trajectories were constructed using latent class growth analysis. Hyperactivity symptoms were based on mother ratings on the hyperactivity subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 10 to 15. A total score was generated based on two items on the subscale for each assessed year, ranging from 0 to 4.

[4] Inattention was assessed by teachers when participants were aged 6 using the inattentiveness subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 8.

[5] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

Table 4.5c. Association between inattention symptom score trajectory (teacher ratings) and heavy cigarette smoking in young adulthood

	Heavy cigarette smoking[1]					
Inattention symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	2.65	(1.53,4.6)	<0.001*	1.95	(1.1,3.45)	0.022*
Moderate trajectory	1.83	(1.07,3.11)	0.027*	1.52	(0.89,2.61)	0.125
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Hyperactivity[4]	-	-	-	1.04	(0.9,1.21)	0.560
Opposition[5]	-	-	-	1.11	(1.02,1.21)	0.012*
Father's occupational prestige[6]	-	-	-	1.00	(0.98,1.01)	0.783

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Heavy cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked the number of cigarettes smoked in the past week. Heavy cigarette smoking was defined as 140 cigarettes (about one pack) or more.

[2] Odds ratios were derived from binomial logistic regressions.

[3] Inattention symptom trajectories were constructed using latent class growth analysis. Inattention symptoms were based on teacer ratings on the inattentiveness subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 6 to 15. A total score was generated based on four items on the subscale for each assessed year, ranging from 0 to 8.

[4] Hyperactivity was assessed by teachers when participants were aged 6 using the hypaeractivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.

[4] Opposition symptoms were based on teacher ratings on the opposition subscale of the SBQ when participants were age 6. A total score was generated based on five items on the subscale for each assessed year, ranging from 0 to 10.

[6] Occupational prestige is defined according to Blishen BR, Carroll WK, and Moore C. (1987). The 1981 socioeconomic index for occupations in Canada. Canadian Review of Sociology, 24(4): 465-488.

Table 4.5d. Association between inattention symptom score trajectory (mother ratings) and heavy cigarette smoking in young adulthood

	Heavy cigarette smoking[1]					
Inattention symptom score trajectory[3]	**Unadjusted OR[2]**	**(95% CI)**	**P-value**	**Adjusted OR[2]**	**(95% CI)**	**P-value**
High trajectory	1.86	(1.11,3.12)	0.019*	1.61	(0.95,2.72)	0.078
Moderate trajectory	1.45	(0.97,2.18)	0.074	1.31	(0.86,1.98)	0.205
Low trajectory	Ref	Ref	Ref	Ref	Ref	Ref
Confounding variables at baseline						
Hyperactivity[4]	-	-	-	1.22	(1.07,1.39)	0.004*

Abbreviation: OR= odds ratio; CI= confidence interval

[1] Heavy cigarette smoking was based on participants' self-reported response to a question in the Questionnaire on the Development of Young Adults, which asked the number of cigarettes smoked in the past week. Heavy cigarette smoking was defined as 140 cigarettes (about one pack) or more.

[2] Odds ratios were derived from binomial logistic regressions.

[3] Inattention symptom trajectories were constructed using latent class growth analysis. Inattention symptoms were based on mother ratings on the inattentiveness subscale on the Social Behavior Questionnaire (SBQ) when participants were ages 10 to 15. A total score was generated based on four items on the subscale for each assessed year, ranging from 0 to 8.

[4] Hyperactivity was assessed by teachers when participants were aged 6 using the hyperactivity subscale of the Social Behavior Questionnaire, with a score that ranged from 0 to 4.

Table 4.6a. Assessment of frequency of cigarette smoking and other substances in late adolescence as a mediator of the association between inattention symptom trajectories (teacher ratings) and daily cigarette smoking in young adulthood

Frequency of cigarette smoking as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Smoking freq = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Smoking freq + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.56	(0.98,2.48)	0.074	1.34	(0.93,1.93)	0.122	3.24	(2.03,5.19)	0.000	1.40	(0.84,2.32)	0.201
High	2.67	(1.58,4.49)	0.001	1.87	(1.27,2.75)	0.002	13.99	(8.25,23.74)	0.000	2.23	(1.25,3.95)	0.011

Frequency of alcohol use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Drinking freq = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Drinking frequency + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq + Drinking freq		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.56	(0.98,2.48)	0.074	1.28	(0.88,1.88)	0.196	1.08	(0.73,1.60)	0.713	1.40	(0.84,2.32)	0.202
High	2.67	(1.58,4.49)	0.001	1.00	(0.68,1.47)	0.993	1.08	(0.73,1.60)	0.713	2.24	(1.26,3.98)	0.011

Frequency of marijuana use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Marijuana use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Marijuana use + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq + MJ use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.56	(0.98,2.48)	0.074	1.80	(1.22,2.65)	0.004	1.12	(0.76,1.67)	0.564	1.38	(0.84,2.27)	0.208
High	2.67	(1.58,4.49)	0.001	2.06	(1.36,3.13)	0.001	1.12	(0.76,1.67)	0.564	2.20	(1.25,3.85)	0.010

Frequency of other drug use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Other drug use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Other drug use + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq + drug use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.56	(0.98,2.48)	0.074	2.54	(1.61,4.02)	0.000	0.86	(0.53,1.40)	0.552	1.43	(0.88,2.33)	0.156
High	2.67	(1.58,4.49)	0.001	3.45	(2.14,5.58)	0.000	0.86	(0.53,1.40)	0.552	2.29	(1.32,3.96)	0.005

Table 4.6b. Assessment of frequency of cigarette smoking and other substance use in late adolescence as a mediator of the association between inattention symptom trajectories (mother ratings) and daily cigarette smoking in young adulthood

Frequency of smoking frequency as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Smoking freq = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Smoking freq + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.72	(1.12,2.62)	0.021	1.40	(1.03,1.91)	0.030	2.84	(1.97,4.09)	0.000	1.59	(0.94,2.67)	0.104
High	2.53	(1.55,4.11)	0.001	1.75	(1.20,2.54)	0.003	12.37	(8.25,18.54)	0.000	2.25	(1.28,3.97)	0.009

Frequency of alcohol use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Drinking freq = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Drinking frequency + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq + Drinking freq		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.72	(1.12,2.62)	0.021	1.01	(0.73,1.40)	0.945	1.09	(0.66,1.80)	0.749	1.59	(0.94,2.67)	0.102
High	2.53	(1.55,4.11)	0.001	1.16	(0.77,1.74)	0.486	1.09	(0.66,1.80)	0.749	2.26	(1.28,3.97)	0.008

Frequency of marijuana use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Marijuana use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Marijuana use + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq + MJ use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.72	(1.12,2.62)	0.021	1.28	(0.91,1.79)	0.164	1.37	(0.86,2.19)	0.207	1.59	(0.94,2.69)	0.106
High	2.53	(1.55,4.11)	0.001	1.31	(0.87,1.96)	0.193	1.37	(0.86,2.19)	0.207	2.26	(1.28,4.02)	0.009

Frequency of drug use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Other drug use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Other drug use + Ina trajectory			Step 4 (Testing path c') Model: Daily smoking = Ina trajectory + Smoking freq + Drug use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.72	(1.12,2.62)	0.021	1.32	(0.89,1.95)	0.170	0.97	(0.63,1.50)	0.886	1.59	(0.94,2.67)	0.102
High	2.53	(1.55,4.11)	0.001	1.42	(0.88,2.28)	0.152	0.97	(0.63,1.50)	0.886	2.26	(1.28,3.96)	0.008

Table 4.7a. Assessment of frequency of cigarette smoking and other substance use in late adolescence as a mediator of the association between inattention symptom trajectories (teacher ratings) and heavy cigarette smoking in young adulthood

Frequency of smoking frequency as potential mediator

	Step 1 (Testing path c) Model: Heavy smoking = Ina trajectory			Step 2 (Testing path a) Model: Smoking freq = Ina trajectory			Step 3 (Testing path b) Model: Heavy smoking = Smoking freq + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.52	(0.89,2.61)	0.125	1.34	(0.93,1.93)	0.122	1.97	(1.09,3.54)	0.031	1.38	(0.77,2.45)	0.282
High	1.95	(1.11,3.43)	0.022	1.87	(1.27,2.75)	0.002	5.92	(3.56,9.84)	0.000	1.50	(0.76,2.96)	0.248

Frequency of alcohol use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Drinking freq = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Drinking frequency + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq + Drinking		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.52	(0.89,2.61)	0.125	1.28	(0.88,1.88)	0.196	0.89	(0.59,1.33)	0.558	1.38	(0.77,2.46)	0.281
High	1.95	(1.11,3.43)	0.022	1.00	(0.68,1.47)	0.993	0.89	(0.59,1.33)	0.558	1.48	(0.75,2.93)	0.267

Frequency of marijuana use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Marijuana use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Marijuana use + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq + MJ use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.52	(0.89,2.61)	0.125	1.80	(1.22,2.65)	0.004	1.25	(0.74,2.12)	0.410	1.35	(0.75,2.44)	0.318
High	1.95	(1.11,3.43)	0.022	2.06	(1.36,3.13)	0.001	1.25	(0.74,2.12)	0.410	1.48	(0.74,2.96)	0.270

Frequency of drug use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Other drug use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Other drug use + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq + Drug use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.52	(0.89,2.61)	0.125	2.54	(1.61,4.02)	0.000	1.17	(0.78,1.78)	0.450	1.34	(0.74,2.43)	0.329
High	1.95	(1.11,3.43)	0.022	3.45	(2.14,5.58)	0.000	1.17	(0.78,1.78)	0.450	1.46	(0.73,2.92)	0.291

Table 4.7b. Assessment of frequency of cigarette smoking and other substance use in late adolescence as a mediator of the association between inattention symptom trajectories (mother ratings) and heavy cigarette smoking in young adulthood

Frequency of smoking frequency as potential mediator

	Step 1 (Testing path c) Model: Heavy smoking = Ina trajectory			Step 2 (Testing path a) Model: Smoking freq = Ina trajectory			Step 3 (Testing path b) Model: Heavy smoking = Smoking freq + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.31	(0.86,1.98)	0.205	1.40	(1.03,1.91)	0.030	1.79	(0.93,3.47)	0.103	1.11	(0.71,1.73)	0.654
High	1.61	(0.95,2.71)	0.078	1.75	(1.20,2.54)	0.003	5.33	(3.25,8.76)	0.000	1.26	(0.71,2.22)	0.428

Frequency of alcohol use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Drinking freq = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Drinking frequency + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq + Drinking		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.31	(0.86,1.98)	0.205	1.01	(0.73,1.40)	0.945	0.90	(0.61,1.35)	0.621	1.10	(0.71,1.72)	0.660
High	1.61	(0.95,2.71)	0.078	1.16	(0.77,1.74)	0.486	0.90	(0.61,1.35)	0.621	1.26	(0.71,2.22)	0.434

Frequency of marijuana use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Marijuana use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Marijuana use + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq + MJ use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.31	(0.86,1.98)	0.205	1.28	(0.91,1.79)	0.164	1.31	(0.85,2.02)	0.226	1.11	(0.71,1.72)	0.657
High	1.61	(0.95,2.71)	0.078	1.31	(0.87,1.96)	0.193	1.31	(0.85,2.02)	0.226	1.27	(0.72,2.25)	0.410

Frequency of drug use as potential mediator

	Step 1 (Testing path c) Model: Daily smoking = Ina trajectory			Step 2 (Testing path a) Model: Other drug use = Ina trajectory			Step 3 (Testing path b) Model: Daily smoking = Other drug use + Ina trajectory			Step 4 (Testing path c') Model: Heavy smoking = Ina trajectory + Smoking freq + Drug use		
	OR	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Inattention symptom score trajectory												
Moderate	1.31	(0.86,1.98)	0.205	1.32	(0.89,1.95)	0.170	1.19	(0.75,1.90)	0.460	1.11	(0.71,1.72)	0.660
High	1.61	(0.95,2.71)	0.078	1.42	(0.88,2.28)	0.152	1.19	(0.75,1.90)	0.460	1.26	(0.71,2.23)	0.425

Figure 4.1 Four components of mediation analysis, as proposed by Baron and Kenny[52]

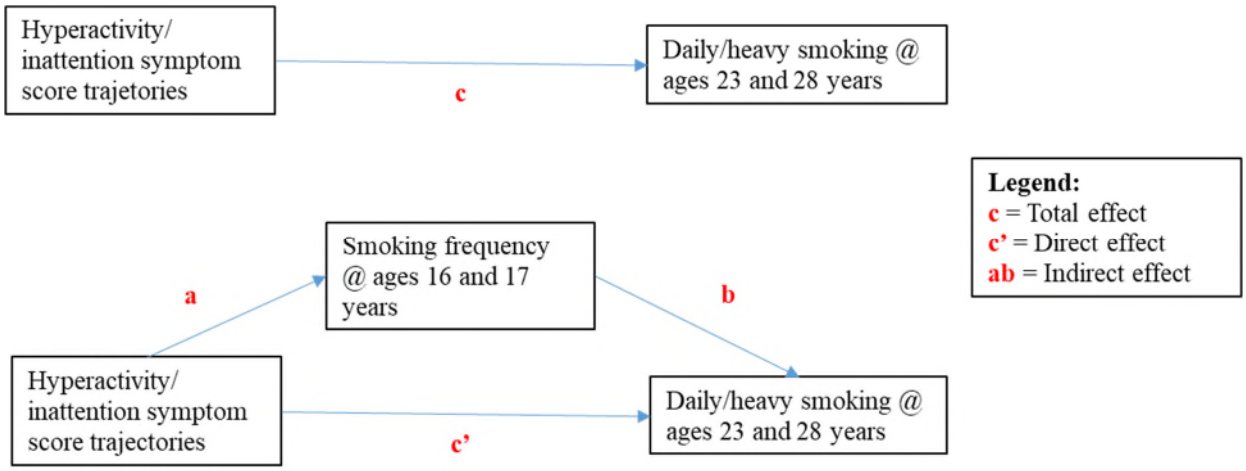


Figure 4.2a. Directed acyclic graph of theoretical framework for the association of hyperactivity symptom score trajectory (teacher ratings) with cigarette smoking frequency in late adolescence

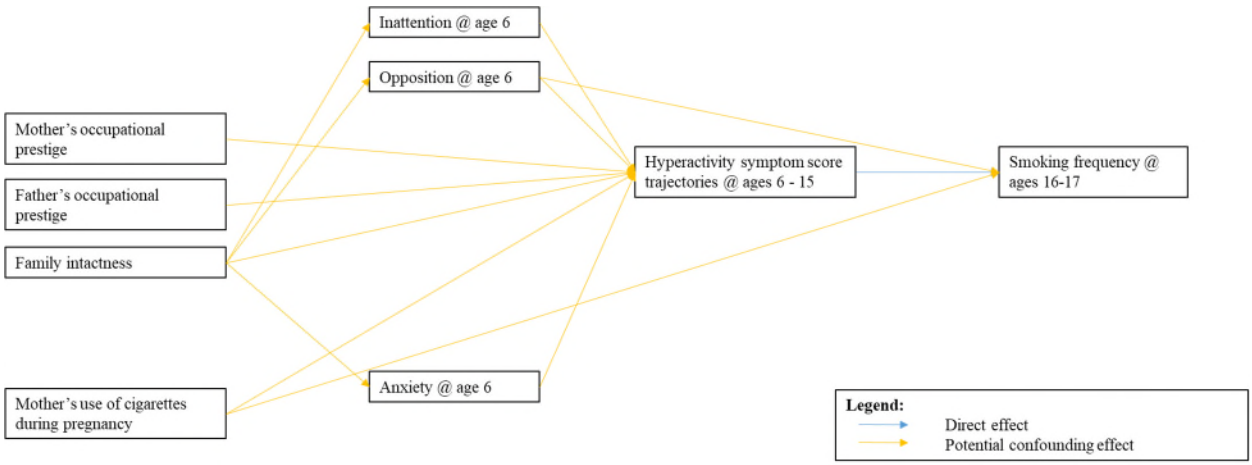


Figure 4.2b. Directed acyclic graph of theoretical framework for the association of hyperactivity symptom score trajectory (teacher ratings) with daily cigarette smoking in young adulthood

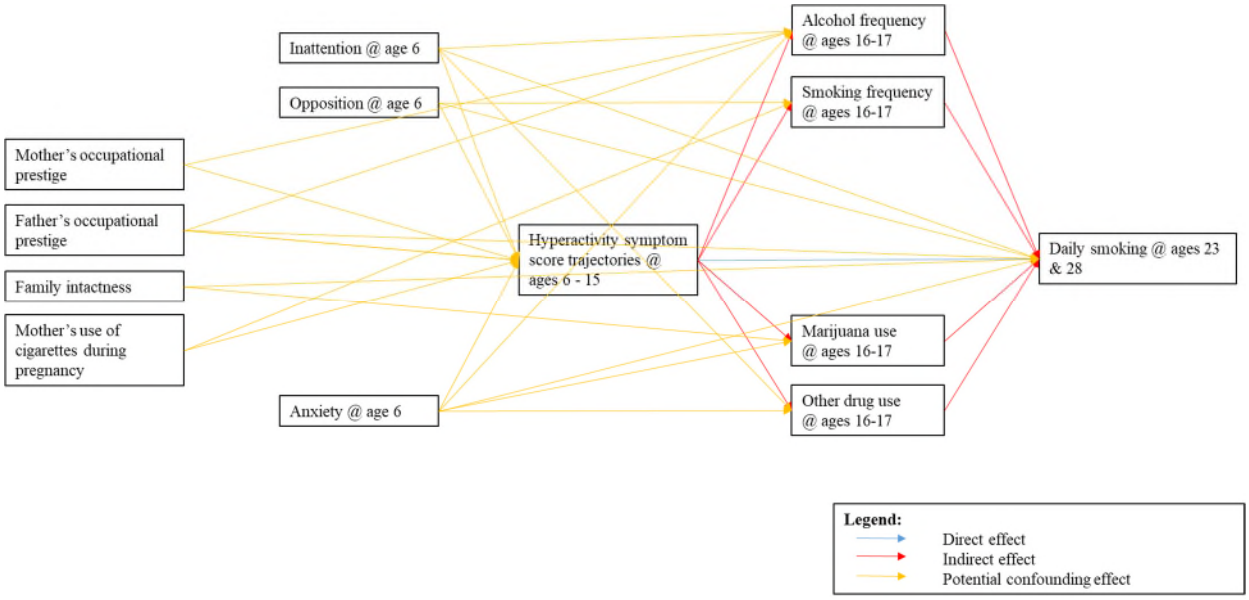


Figure 4.2c. Directed acyclic graph of theoretical framework for the association of hyperactivity symptom score trajectory (teacher ratings) with heavy cigarette smoking in young adulthood

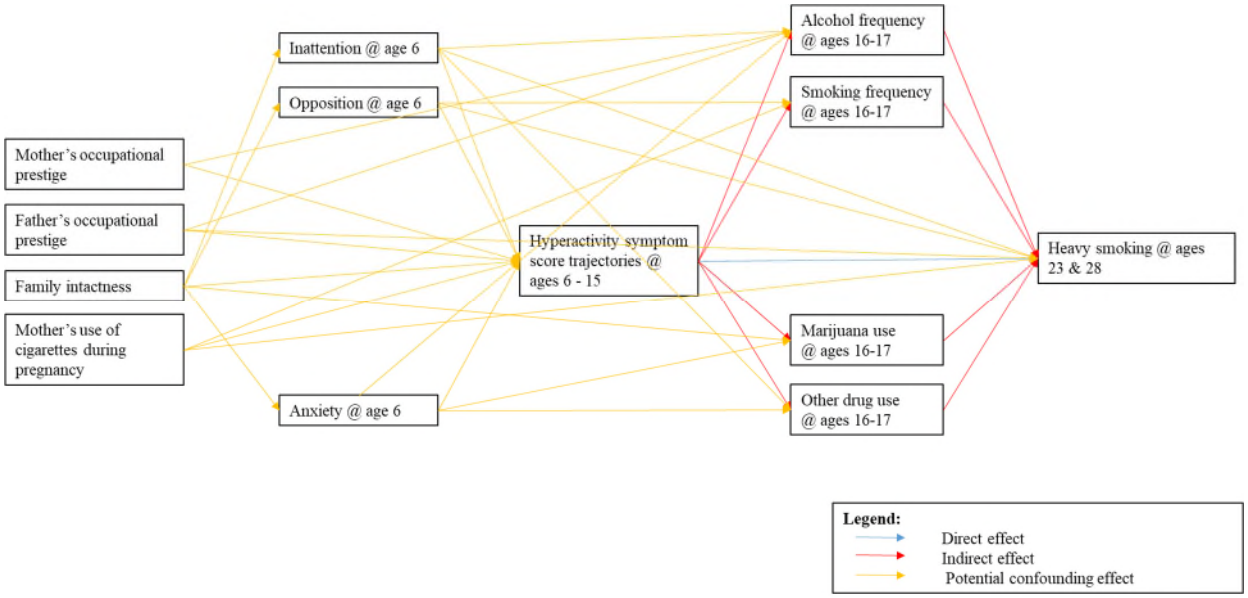


Figure 4.2d. Directed acyclic graph of theoretical framework for the association of inattention symptom score trajectory (teacher ratings) with cigarette smoking frequency in late adolescence

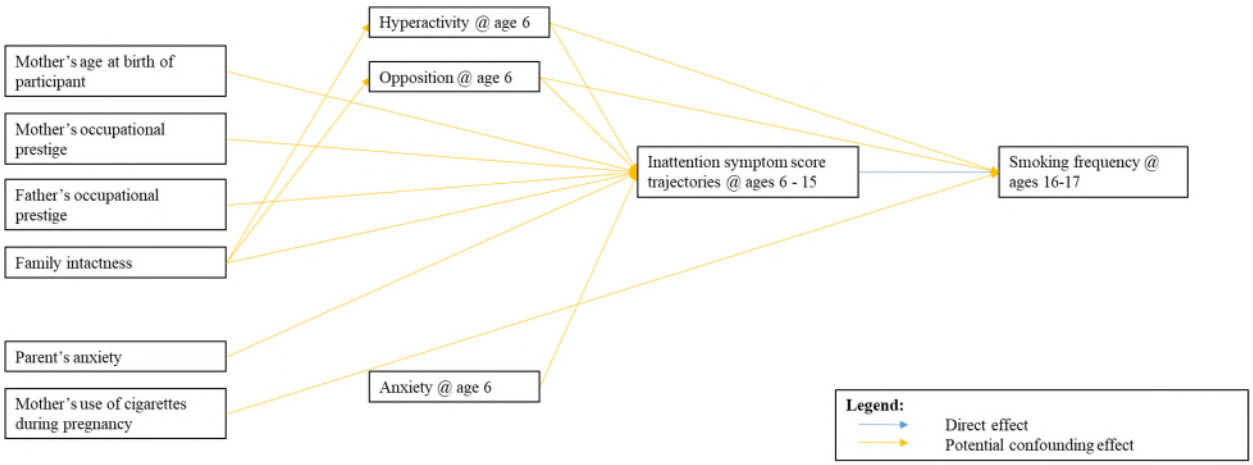


Figure 4.2d. Directed acyclic graph of theoretical framework for the association of inattention symptom score trajectory (teacher ratings) with daily cigarette smoking in young adulthood

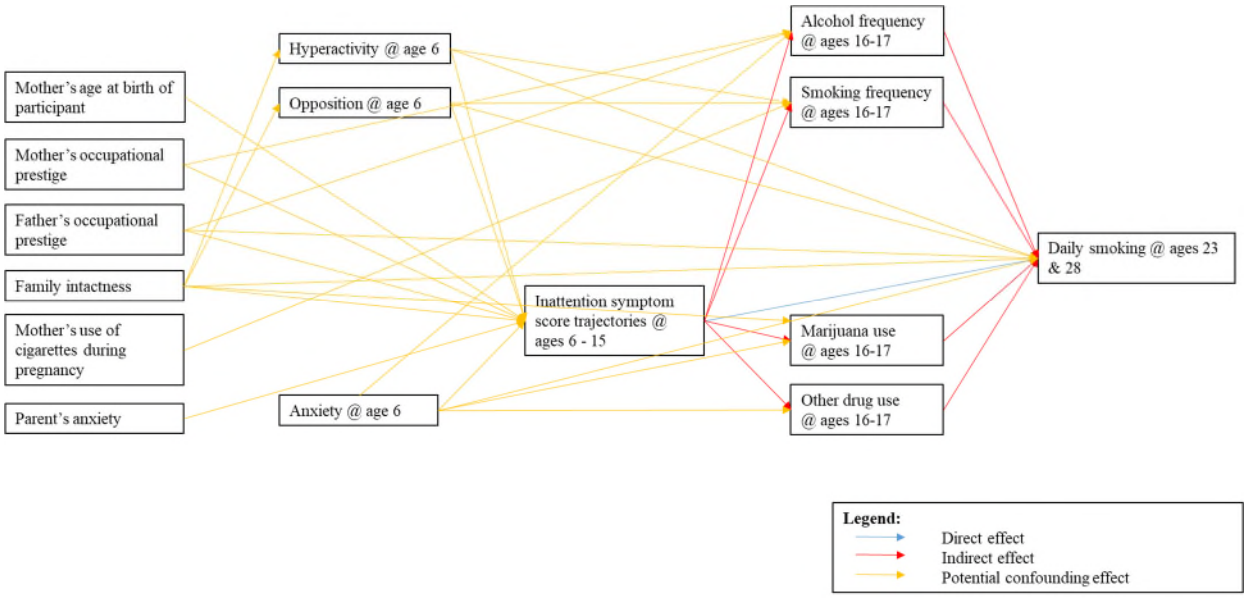
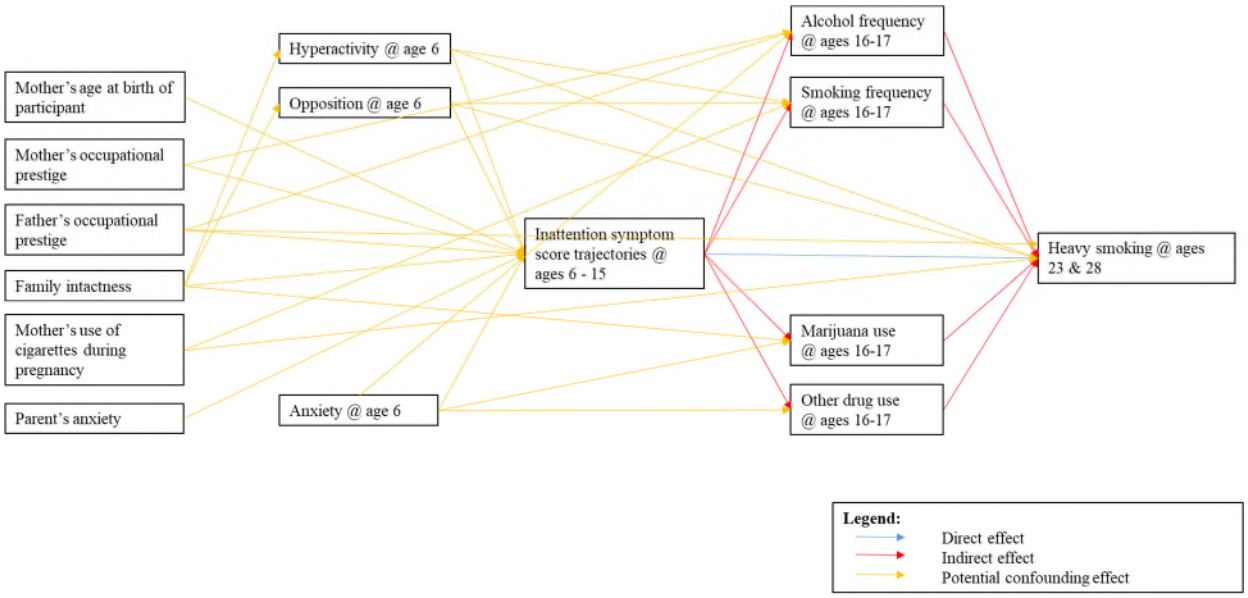


Figure 4.2f. Directed acyclic graph of theoretical framework for the association of inattention symptom score trajectory (teacher ratings) with heavy cigarette smoking in young adulthood



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CHAPTER 5
Conclusion

Increasing evidence suggests that childhood ADHD and its symptom domains--hyperactivity and inattention—often persist to adolescence and later years, although symptoms may wax and wane over time.[1-10] The adoption of trajectory analytic methods in recent decades has allowed investigators to trace the developmental courses of ADHD and its symptom domains comprehensively, and to identify individual differences in symptom courses within various samples.[11-20] The many health risks associated with childhood ADHD include cigarette smoking in adolescence.[21-26] However, this risk of cigarette smoking may differ by symptom domain and symptom trajectory, and such differences have rarely been studied.

For my dissertation research, I analyzed the symptom score trajectories of hyperactivity and inattention in a cohort study of 1,037 boys from low socioeconomic neighborhoods in Montreal, Canada. Data were obtained from the Longitudinal and Experimental Study of Low Socioeconomic Status Boys (ELEM), which was designed to assess the social development in a population of economically disadvantaged boys in Montreal.[27] I identified risk factors of different trajectories and examined the risks of cigarette smoking outcomes in adolescence and young adulthood. In this chapter, I summarize the findings from this dissertation research, describe their public health implications, and suggest future directions.

Summary of findings

In Chapter 2, I reviewed the literature on the persistence of symptoms of childhood ADHD and its symptom domains into adolescence, and their associations with cigarette smoking outcomes in adolescence and young adulthood. The literature suggested that childhood ADHD and hyperactivity frequently persisted into adolescence and that their symptom scores followed trajectories that were variously categorized as high, high declining, moderate declining, moderate, low increasing, or low. The proportion of children who had persistent inattention in

adolescence was unknown, but inattention symptom scores typically followed three trajectories that were relatively stable over time--high, moderate, or low. Most individuals presented with chronically low symptom scores for ADHD and its symptom domains, but approximately 13% to 16% continued to have high symptom scores as they aged. Factors that appeared to affect persistence estimates and symptom score trajectories included gender and informant type. Males appeared to be more likely than females and children in the general population to follow a high symptom score trajectory. In rating children's hyperactivity and inattention symptoms, teachers and caregivers appeared to provide different perspectives, which may have affected persistence estimates.

Cigarette smoking in young adulthood was associated with high symptom scores, especially for inattention.

Through my systematic narrative review, I identified gaps in the literature, including a need to expand the research on smoking outcomes in both adolescence and young adulthood, in relation to high childhood symptom trajectories; a need for data on at-risk populations, such as boys of low socioeconomic status; and a need to account for different informants' unique perspectives in assessing symptom persistence.

In Chapter 3, I reported findings from my latent class growth analysis of data from the cohort study of boys from low socioeconomic backgrounds. I derived symptom score trajectories of hyperactivity and inattention between childhood and mid-adolescence based on teachers' and mothers' annual ratings, separately. I also reported on my analysis of risk factors for these symptom score trajectories. Both hyperactivity and inattention symptom scores appeared to follow three trajectories that differed by baseline scores--high, moderate, and low. Hyperactivity symptom scores generally declined over time, whereas inattention symptom scores stayed

relatively stable. Most of the boys had low symptom score trajectories for both domains, but approximately 20% and 33% had high symptom score trajectories for hyperactivity and inattention, respectively. These proportions were higher than those seen in general populations. Mothers scored hyperactivity or inattention symptoms higher than teachers, perhaps because of their different perspectives or because the boys' behavior differed between home and school. The strongest risk factors for high hyperactivity and inattention symptom score trajectories were boys' hyperactivity, inattention, opposition, and anxiety symptom scores at age 6 years (scored only by teachers), and lack of family intactness.

In Chapter 4, I presented results from my study of the associations of hyperactivity and inattention symptom score trajectories with cigarette smoking frequency in late adolescence and daily and heavy (≥1 pack/day) cigarette smoking in young adulthood. I further investigated whether cigarette smoking frequency and frequency of alcohol, marijuana, and other drug use in late adolescence may mediate the associations of symptom score trajectories with cigarette smoking outcomes in young adulthood. To account for different informants' unique perspectives, I analyzed the symptom score trajectories based on teachers' and mothers' ratings, separately. I found that high (vs. low) symptom score trajectories of both hyperactivity and inattention were associated with high frequency of cigarette smoking (≥40 times in the past year) in late adolescence. High symptom score trajectory for inattention, but not for hyperactivity, was also associated with daily and heavy cigarette smoking in young adulthood. Part of this association was mediated by high cigarette frequency in late adolescence. In other words, boys in the high (vs. low) inattention symptom score trajectory group were more likely to smoke cigarettes at high frequency in late adolescence, and to engage in daily and heavy smoking as young adults.

This study is one of the first to document associations of symptom score trajectories of hyperactivity and inattention with smoking outcomes that are plausible for (late) adolescents and young adults. Prior data on symptom score trajectories and smoking outcomes have focused on nicotine abuse or dependence--outcomes that may be too rare to assess in young populations. High symptom levels of inattention (vs. hyperactivity), in particular, seem to confer longer-term risk on problematic cigarette smoking behaviors, especially among individuals who are frequent smokers in late adolescence.

Public health implications

My dissertation research expanded the current understanding of the developmental courses of hyperactivity and inattention symptoms, with a focus on a demographic group--boys from low socioeconomic backgrounds—in which the prevalence of such symptoms is high and has previously received little attention. Although the number of symptom score trajectories and trends (declining for hyperactivity and stable for inattention) among these boys were similar to that in the general population samples, these boys had a higher likelihood of exhibiting high symptom scores of either symptom domain over time. High symptom score trajectories of hyperactivity and inattention were associated with frequent cigarette smoking in adolescence (see Chapter 4). High symptom score trajectory of inattention was also linked to daily and heavy cigarette smoking in young adulthood. Socioeconomically disadvantaged boys therefore represent a vulnerable population that may benefit from behavioral interventions to manage and reduce their hyperactivity and inattention symptoms. In particular, boys with high symptom scores of hyperactivity, inattention, opposition, and anxiety at age 6 years were at increased risk of high symptom score trajectories of hyperactivity and inattention at ages 10-15 years (see chapter 3), suggesting that these subgroups of boys may benefit the most from behavioral

interventions. Additionally and notably, lack of family intactness was found to be a risk factor for high symptom score trajectories of both hyperactivity and inattention. This finding underscores the importance of family environment for proper child development. Therefore, interventions to reduce and manage hyperactivity and inattention symptom should not be limited to behavioral efforts focusing on the children alone, but should also take into account the children's environment. Increased support for non-intact families with children may be beneficial for hyperactivity and inattention symptom control and their adverse health outcomes, perhaps especially among socioeconomically disadvantaged boys.

The study described in Chapter 4 indicated that boys in the high (vs. low) trajectories in either symptom domain were at nearly doubled risk of frequent cigarette smoking in late adolescence, and that high symptom score trajectory of inattention, but not hyperactivity, was further associated with problematic smoking behaviors in young adulthood. These findings may suggest that the mechanisms underlying the urge to smoke differ given high symptom score trajectories of hyperactivity vs. inattention. Perhaps for boys with high hyperactivity symptom scores, frequent cigarette smoking in late adolescence was a product of amplified behavioral disinhibition or lack of self-control.[28-30] As for boys with high inattention symptom scores, smoking may have involved self-medication with nicotine for attention deficits.[31-34] Because hyperactivity symptoms tended to dissipate over time, whereas inattention symptoms generally did not, by the time the boys became young adults, the impulse to engage in high levels of smoking may have dissipated along with their hyperactivity symptoms. As inattention remained stable over time, the need for stimulation from nicotine also remained.

In light of these findings, as proposed above, behavioral interventions may be needed to help boys who have high symptom levels of hyperactivity and, particularly, inattention. If self-

medication is indeed the driving force behind smoking among children with inattention, alternative coping strategies or proper medications might be recommended to them. Public health smoking prevention and cessation program developers should consider targeting individuals with histories of as well as high and persistent levels of hyperactivity and inattention symptoms. Behavioral interventions to manage hyperactivity and inattention symptoms might help to prevent or reduce smoking in adolescence and later life.

Future directions

My dissertation research is one of the first research efforts to assess symptom score trajectories of hyperactivity and inattention in boys from low socioeconomic backgrounds and to investigate the associations of high symptom score trajectories of hyperactivity and inattention with frequency of cigarette smoking in late adolescence and daily and heavy cigarette smoking in young adulthood. Because data on this demographic group and on the understanding of symptom score trajectories and smoking behaviors are sorely lacking, future studies are warranted to replicate and further the findings from this research. Based on what I have learned from my research, I recommend a few specific future directions as follows.

First, hyperactivity and inattention symptom scores were based on the Social Behavioral Questionnaire (SBQ), which is very short, has only a few items on hyperactivity and inattention symptoms, and does not account for symptom-related impairments. Although SBQ's brevity makes it easy to use for annual assessments and with different informants, it assesses only a limited range of symptoms. As future studies continue to evaluate hyperactivity and inattention symptom score trajectories, other instruments that may account for different informants' ratings (in order to account for unique perspectives and situational differences) with more detailed symptom lists should be considered.

Second, in my assessment of the associations of symptom score trajectories with cigarette smoking outcomes, I focused on frequency of cigarette smoking in late adolescence and daily and heavy cigarette smoking in young adulthood. Other developmentally appropriate cigarette smoking outcomes should be studied; investigators may consider age of smoking initiation, long-term use, and pack years, which are also clinically meaningful and prognostic of later problematic smoking behaviors, for future research.

Third, I conducted all the empirical analyses for my dissertation research on a sample of boys from low socioeconomic neighborhoods. The sample was selected to bring attention to a vulnerable demographic group. However, because the understanding of the associations of symptom score trajectories of hyperactivity and inattention with smoking outcomes remains highly limited, other vulnerable populations should also be investigated.

Finally, latent class growth analysis is one of many trajectory analytic methods that can be used to assess symptom score trajectories. In my dissertation research, I used proc traj in SAS to identify hyperactivity and inattention symptom score trajectories. Identifying the most parsimonious models required both empirical decision rules and subjective evaluations. Other statistical software packages, such as Mplus, provide other strategies to construct trajectories based on more objective decision rules. Their validity and efficiency remain to be assessed, but our understanding of the developmental course of ADHD and its symptom score trajectories may benefit from consideration of these different approaches.

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APPENDIX 1

Table 1. Search terms used in MEDLINE and PsycINFO to identify studies published from 1985 to February 2019

MEDLINE (1985 to February 2019) was searched using the following search terms:
(("attention deficit disorder with hyperactivity"[MeSH Terms] OR (inattention[All Fields] OR inattentive[All Fields] OR ("hyperkinesis"[MeSH Terms] OR "hyperkinesis"[All Fields] OR "hyperactivity"[All Fields]) OR ("hyperkinesis"[MeSH Terms] OR "hyperkinesis"[All Fields] OR "hyperactive"[All Fields]))) AND (persistence[All Fields] OR trajectories[All Fields]))
PsychINFO (1985 to February 2019) was searched using the following search terms:
1. Attention Deficit Disorder with Hyperactivity/ or Attention Deficit Disorder/ 2. (inattention or inattentive or hyperactivity or hyperactive).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] 3. 1 or 2 4. Persistence/ 5. Trajectories.mp. 6. 4 or 5 **7.** 3 and 6

APPENDIX 2

Table 1. Number and proportion of boys with hyperactivity and inattention symptom score ratings per year of age, by teachers and mothers

Boys' age	Teachers	Mothers	Both
Hyperactivity symptom score, n (%)			
6	1,034 (99.7%)	0 (0.0%)	0 (0.0%)
10	973 (93.8%)	701 (67.6%)	668 (64.4%)
11	942 (90.8%)	731 (70.5%)	712 (68.7%)
12	884 (85.2%)	684 (66.0%)	641 (61.8%)
13	817 (78.8%)	635 (61.2%)	578 (55.7%)
14	813 (78.4%)	635 (61.2%)	584 (56.3%)
15	753 (72.6%)	621 (59.9%)	536 (51.7%)
Inattention symptom score, n (%)			
6	1,036 (99.9%)	0 (0.0%)	0 (0.0%)
10	977 (94.2%)	702 (67.7%)	672 (64.8%)
11	942 (90.8%)	730 (70.4%)	711 (68.6%)
12	884 (85.2%)	685 (66.1%)	642 (61.9%)
13	818 (78.9%)	642 (61.9%)	583 (56.2%)
14	815 (78.6%)	644 (62.1%)	593 (57.2%)
15	755 (72.8%)	629 (60.7%)	544 (52.5%)

Table 2a. Tipping point sensitivity analysis to assess impact of violations of the missing at random assumption for mother's occupational prestige and its associated risk for high hyperactivity symptom score trajectory based on teacher ratings

Parameter	Original			Scale=0.60			Scale=0.90			Scale=1.10			Scale=1.12			Scale=1.13		
	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|
High declining trajectory																		
Constant	3.337448	1.196676	0.0058	3.224534	1.173863	0.0063	3.271238	1.150836	0.0046	3.152133	1.189418	0.0087	3.438347	1.153316	0.003	3.45127	1.154122	0.0029
Boy's inattention at baseline	0.597664	0.099505	<.0001	0.60631	0.101237	<.0001	0.62356	0.10353	<.0001	0.604358	0.10006	<.0001	0.61813	0.09873	<.0001	0.616488	0.098732	<.0001
Boy's opposition at baseline	1.055148	0.142953	<.0001	1.10194	0.149233	<.0001	1.086336	0.153006	<.0001	1.053339	0.141644	<.0001	1.044435	0.140644	<.0001	1.042933	0.140223	<.0001
Boy's anxiety at baseline	-0.593143	0.083383	<.0001	-0.618252	0.086988	<.0001	-0.615687	0.086577	<.0001	-0.588059	0.083466	<.0001	-0.596179	0.083663	<.0001	-0.59515	0.083545	<.0001
Mother's age (years) at boy's birth	-0.088807	0.051883	0.0915	-0.081403	0.048964	0.0977	-0.0876	0.049729	0.0795	-0.085923	0.046517	0.0649	-0.089783	0.047382	0.0586	-0.090111	0.047088	0.056
Father's age (years) at boy's birth	0.012328	0.042401	0.7722	0.011725	0.039506	0.7669	0.013919	0.040471	0.7314	0.010221	0.040468	0.8011	0.010857	0.039222	0.7822	0.011089	0.038895	0.7758
Mother's occupational prestige	-0.039662	0.01558	0.0122	-0.043551	0.013841	0.0017	-0.041873	0.015074	0.0059	-0.036674	0.016065	0.0262	-0.03013	0.014757	0.0426	-0.0301	0.014641	0.0411
Father's occupational prestige	-0.041919	0.015084	0.0063	-0.041573	0.014231	0.0036	-0.040585	0.014696	0.0063	-0.043028	0.015799	0.0085	-0.050025	0.014971	0.001	-0.049801	0.014946	0.001
Family intactness	-0.802497	0.380306	0.0353	-0.7359	0.378108	0.0518	-0.791645	0.385648	0.0406	-0.741029	0.377424	0.0501	-0.815228	0.367857	0.0267	-0.829275	0.367663	0.0242
Parent's depression	-0.617547	0.721847	0.4023	-0.216502	0.771863	0.7833	-0.115275	0.581317	0.8431	0.105318	0.666434	0.8761	-0.245458	0.587201	0.6769	-0.306347	0.571744	0.5931
Parent's anxiety	1.84909	0.788719	0.0283	1.516353	0.711533	0.0383	1.627391	0.678506	0.018	1.051703	0.904135	0.2691	1.401103	0.775131	0.0832	1.463446	0.700424	0.0424
Mother's use of cigarettes during pregnancy	0.307967	0.308001	0.3174	0.311134	0.311145	0.3173	0.310955	0.311202	0.3177	0.304643	0.30474	0.3175	0.304436	0.304491	0.3174	0.304803	0.304841	0.3174

[1] All estimates shown are multinomial logit coefficients derived from multivariate latent class regression

Table 2b. Tipping point sensitivity analysis to assess impact of violations of the missing at random assumption for father's occupational prestige and its associated risk for high hyperactivity symptom score trajectory based on teacher ratings

Parameter	Original			Scale=0.80			Scale=0.90			Scale=1.10			Scale=1.30			Scale=1.31		
	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|
High declining trajectory																		
Constant	3.337448	1.196676	0.0058	2.955701	1.152965	0.0107	3.389219	1.223598	0.0064	3.259305	1.198515	0.0072	3.46044	1.344492	0.0137	3.156915	1.21012	0.0097
Boy's inattention at baseline	0.597664	0.099505	<.0001	0.606694	0.101705	<.0001	0.611318	0.099615	<.0001	0.614559	0.09863	<.0001	0.59409	0.103146	<.0001	0.622317	0.100981	<.0001
Boy's opposition at baseline	1.055148	0.142953	<.0001	1.066644	0.145713	<.0001	1.066035	0.146164	<.0001	1.054052	0.145409	<.0001	0.999055	0.16838	<.0001	1.07355	0.151694	<.0001
Boy's anxiety at baseline	-0.593143	0.083383	<.0001	-0.593624	0.083764	<.0001	-0.600315	0.084061	<.0001	-0.598607	0.083919	<.0001	-0.571573	0.094674	<.0001	-0.600026	0.08572	<.0001
Mother's age (years) at boy's birth	-0.088807	0.051883	0.0915	-0.080241	0.047708	0.0932	-0.08773	0.048846	0.0739	-0.09613	0.046733	0.0399	-0.085091	0.046407	0.0669	-0.092937	0.046501	0.0457
Father's age (years) at boy's birth	0.012328	0.042401	0.7722	0.007047	0.038484	0.8548	0.00972	0.039436	0.8055	0.01755	0.038172	0.6458	0.001849	0.038341	0.9615	0.017597	0.037691	0.6406
Mother's occupational prestige	-0.039662	0.01558	0.0122	-0.033218	0.018586	0.0877	-0.039685	0.016233	0.0172	-0.038843	0.015712	0.0153	-0.043087	0.015492	0.0067	-0.046376	0.014525	0.0015
Father's occupational prestige	-0.041919	0.015084	0.0063	-0.04237	0.014315	0.0033	-0.041727	0.014502	0.0042	-0.038533	0.016899	0.0304	-0.025598	0.012384	0.0388	-0.025437	0.014293	0.0814
Family intactness	-0.802497	0.380306	0.0353	-0.670498	0.374908	0.0739	-0.764693	0.380728	0.0448	-0.817403	0.39561	0.0405	-0.891923	0.411501	0.0326	-0.953293	0.393342	0.0161
Parent's depression	-0.617547	0.721847	0.4023	-0.31807	0.761479	0.6824	-0.153759	0.724596	0.8343	-0.318751	0.690666	0.6487	-0.25551	0.87705	0.7771	-0.146832	0.836278	0.8641
Parent's anxiety	1.84909	0.788719	0.0283	1.519945	0.743362	0.0489	1.320421	0.815457	0.1229	1.458507	0.724664	0.0513	1.462314	1.034559	0.1911	1.371089	0.891613	0.1514
Mother's use of cigarettes during pregnancy	0.307967	0.308001	0.3174	0.305861	0.305894	0.3174	0.310161	0.310212	0.3174	0.30835	0.308426	0.3174	0.305685	0.305781	0.3175	0.310895	0.310922	0.3174

[1] All estimates shown are multinomial logit coefficients derived from multivariate latent class regression

Table 2c. Tipping point sensitivity analysis to assess impact of violations of the missing at random assumption for parent's anxiety and its associated risk for high hyperactivity symptom score trajectory based on teacher ratings

	Original			Scale=0.90			Scale=0.91			Scale=1.03			Scale=1.04			Scale=1.10		
Parameter	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**
High declining trajectory																		
Constant	3.337448	1.196676	0.0058	3.370306	1.167039	0.0041	3.556942	1.160324	0.0023	3.162426	1.128681	0.0051	3.38693	1.172235	0.0041	3.258218	1.154962	0.005
Boy's inattention at baseline	0.597664	0.099505	<.0001	0.612914	0.098972	<.0001	0.612367	0.099425	<.0001	0.612638	0.098985	<.0001	0.619692	0.101637	<.0001	0.60662	0.099326	<.0001
Boy's opposition at baseline	1.055148	0.142953	<.0001	1.051841	0.142265	<.0001	1.058087	0.144452	<.0001	1.069876	0.1453	<.0001	1.062031	0.144449	<.0001	1.081544	0.150131	<.0001
Boy's anxiety at baseline	-0.593143	0.083383	<.0001	-0.594645	0.083856	<.0001	-0.595674	0.084503	<.0001	-0.597682	0.084434	<.0001	-0.596515	0.083247	<.0001	-0.600831	0.085678	<.0001
Mother's age (years) at boy's birth	-0.088807	0.051883	0.0915	-0.09078	0.047362	0.0559	-0.085911	0.049435	0.0842	-0.087916	0.046723	0.06	-0.084329	0.047271	0.0748	-0.089802	0.046101	0.0514
Father's age (years) at boy's birth	0.012328	0.042401	0.7722	0.01384	0.037458	0.7118	0.006354	0.039785	0.8733	0.012335	0.037603	0.7429	0.009335	0.038543	0.8087	0.014925	0.038075	0.6952
Mother's occupational prestige	-0.039662	0.01558	0.0122	-0.040013	0.015398	0.0104	-0.039407	0.015703	0.0138	-0.037862	0.01521	0.0137	-0.041541	0.014343	0.0038	-0.041482	0.016809	0.0175
Father's occupational prestige	-0.041919	0.015084	0.0063	-0.041277	0.015182	0.0075	-0.042598	0.015783	0.0088	-0.041573	0.014762	0.0054	-0.038261	0.014564	0.0094	-0.040714	0.013937	0.0036
Family intactness	-0.802497	0.380306	0.0353	-0.802675	0.371576	0.0308	-0.823068	0.380217	0.0308	-0.74059	0.364652	0.0423	-0.798486	0.377711	0.0348	-0.739242	0.371554	0.0467
Parent's depression	-0.617547	0.721847	0.4023	-0.444584	0.618065	0.4733	-0.38899	0.591167	0.511	-0.188461	0.612448	0.7599	-0.140573	0.643473	0.8289	-0.228392	0.700674	0.7481
Parent's anxiety	1.84909	0.788719	0.0283	1.456582	0.754742	0.0585	1.458877	0.644335	0.0236	1.380925	0.66383	0.0416	1.072229	0.715314	0.1438	1.438502	0.863772	0.1197
Mother's use of cigarettes during pregnancy	0.307967	0.308001	0.3174	0.306406	0.306478	0.3174	0.30864	0.308667	0.3174	0.306367	0.306405	0.3174	0.309076	0.309138	0.3174	0.306064	0.306139	0.3174

[1] All estimates shown are multinomial logit coefficients derived from multivariate latent class regression

Table 3a. Tipping point sensitivity analysis to assess impact of violations of the missing at random assumption for mother's occupational prestige and its associated risk for high inattention symptom score trajectory based on teacher ratings

	Original			Scale=0.60			Scale=0.90			Scale=1.38			Scale=1.39			Scale=1.40		
Parameter	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**
High trajectory																		
Constant	3.849038	1.029431	0.0002	3.845388	1.027419	0.0002	3.876065	1.081762	0.0004	3.371375	1.029557	0.0011	3.465331	1.055059	0.0012	3.120699	1.023255	0.0025
Boy's inattention at baseline	0.6122	0.126291	<.0001	0.618132	0.129871	<.0001	0.619611	0.128185	<.0001	0.619142	0.127357	<.0001	0.620979	0.127142	<.0001	0.612922	0.124729	<.0001
Boy's opposition at baseline	0.281476	0.080206	0.0005	0.282322	0.080746	0.0005	0.281147	0.081339	0.0006	0.274361	0.078832	0.0005	0.272491	0.078786	0.0005	0.272438	0.077655	0.0005
Boy's anxiety at baseline	0.130185	0.050978	0.0107	0.117746	0.050943	0.0208	0.123527	0.050538	0.0145	0.138937	0.050198	0.0056	0.138553	0.050042	0.0056	0.146404	0.05122	0.0043
Mother's age (years) at boy's birth	-0.110079	0.03897	0.0047	-0.112963	0.03976	0.0046	-0.10856	0.039464	0.006	-0.121796	0.040198	0.0026	-0.121835	0.039639	0.0022	-0.112108	0.039263	0.0044
Father's age (years) at boy's birth	0.051741	0.033216	0.1195	0.058741	0.033185	0.0769	0.051818	0.033205	0.1188	0.057782	0.033143	0.0818	0.058008	0.033004	0.0793	0.050147	0.034756	0.1513
Mother's occupational prestige	-0.041967	0.012635	0.0012	-0.047629	0.011899	<.0001	-0.045973	0.011928	0.0001	-0.02414	0.011017	0.031	-0.0229	0.011065	0.0422	-0.015717	0.011101	0.1627
Father's occupational prestige	-0.032244	0.011175	0.0046	-0.028806	0.010652	0.0072	-0.030844	0.010257	0.0027	-0.033858	0.010899	0.0024	-0.035222	0.010916	0.0016	-0.040627	0.011011	0.0004
Family intactness	-0.969334	0.368479	0.0085	-0.979824	0.368796	0.0079	-0.946082	0.380014	0.013	-1.015414	0.380774	0.0078	-1.063736	0.378746	0.005	-0.910404	0.369716	0.0139
Parent's depression	-0.05232	0.414543	0.8999	-0.033804	0.404037	0.9334	0.05878	0.449514	0.8967	-0.087128	0.413819	0.8338	-0.160167	0.389732	0.6816	-0.009109	0.374766	0.9806
Parent's anxiety	0.997381	0.485559	0.0411	0.812333	0.558476	0.1544	0.750193	0.619373	0.2416	0.934784	0.501388	0.0655	0.962729	0.515763	0.067	0.95922	0.568037	0.1037
Mother's use of cigarettes during pregnancy	0.254071	0.254191	0.3175	0.254261	0.254329	0.3174	0.258333	0.25845	0.3175	0.252335	0.252522	0.3177	0.251551	0.251853	0.3179	0.252497	0.252703	0.3177

[1] All estimates shown are multinomial logit coefficients derived from multivariate latent class regression

Table 3b. Tipping point sensitivity analysis to assess impact of violations of the missing at random assumption for father's occupational prestige and its associated risk for high inattention symptom score trajectory based on teacher ratings

	Original			Scale=0.80			Scale=0.90			Scale=1.10			Scale=1.19			Scale=1.20		
Parameter	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**
High trajectory																		
Constant	3.337448	1.196676	0.0058	3.826136	1.096792	0.0006	3.633099	1.101409	0.0013	3.479938	1.089748	0.0017	3.915793	1.021576	0.0001	3.855074	1.010646	0.0001
Boy's inattention at baseline	0.597664	0.099505	<.0001	0.617511	0.128594	<.0001	0.617903	0.126916	<.0001	0.634758	0.131446	<.0001	0.613599	0.129863	<.0001	0.624758	0.127341	<.0001
Boy's opposition at baseline	1.055148	0.142953	<.0001	0.286627	0.080391	0.0004	0.282857	0.079146	0.0004	0.270079	0.080435	0.0008	0.267588	0.079988	0.0008	0.263759	0.079545	0.0009
Boy's anxiety at baseline	-0.593143	0.083383	<.0001	0.122796	0.050856	0.0158	0.126158	0.050944	0.0133	0.130832	0.050743	0.0099	0.133664	0.051723	0.0098	0.133389	0.050945	0.0089
Mother's age (years) at boy's birth	-0.088807	0.051883	0.0915	-0.105378	0.039767	0.0081	-0.104419	0.039776	0.0088	-0.100087	0.039946	0.0124	-0.115414	0.040737	0.0048	-0.112473	0.038823	0.0038
Father's age (years) at boy's birth	0.012328	0.042401	0.7722	0.051737	0.032921	0.1161	0.052499	0.034505	0.1294	0.047962	0.033885	0.1575	0.055005	0.0351	0.1185	0.052232	0.03261	0.1093
Mother's occupational prestige	-0.039662	0.01558	0.0122	-0.043178	0.012475	0.0007	-0.041198	0.012168	0.0008	-0.047727	0.011685	<.0001	-0.048873	0.012175	<.0001	-0.048809	0.01166	<.0001
Father's occupational prestige	-0.041919	0.015084	0.0063	-0.036488	0.010417	0.0005	-0.035	0.010479	0.0009	-0.023772	0.010727	0.0281	-0.0224	0.01041	0.0325	-0.020725	0.010601	0.0531
Family intactness	-0.802497	0.380306	0.0353	-0.886086	0.373777	0.0178	-0.885883	0.381975	0.0208	-0.942146	0.377592	0.0128	-1.08915	0.37769	0.0039	-1.084454	0.380552	0.0045
Parent's depression	-0.617547	0.721847	0.4023	0.167628	0.426292	0.6956	0.036793	0.454846	0.9361	0.016739	0.451934	0.9707	0.075199	0.38413	0.845	0.034417	0.360677	0.924
Parent's anxiety	1.84909	0.788719	0.0283	0.867424	0.497903	0.083	0.951479	0.608693	0.1325	1.049005	0.692124	0.1529	1.082847	0.569877	0.0648	1.062521	0.53596	0.0529
Mother's use of cigarettes during pregnancy	0.307967	0.308001	0.3174	0.255285	0.255378	0.3175	0.256278	0.256543	0.3178	0.256869	0.256922	0.3174	0.254695	0.254809	0.3175	0.252473	0.252676	0.3177

[1] All estimates shown are multinomial logit coefficients derived from multivariate latent class regression

Table 3c. Tipping point sensitivity analysis to assess impact of violations of the missing at random assumption for father's occupational prestige and its associated risk for high inattention symptom score trajectory based on teacher ratings

Parameter	Original			Scale=0.90			Scale=0.99			Scale=1.01			Scale=1.02			Scale=1.03		
	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|	Estimate[1]	Std Error	Pr > |t|
High trajectory																		
Constant	3.337448	1.196676	0.0058	3.872179	1.095565	0.0005	4.025356	1.058983	0.0002	3.996643	1.038328	0.0001	3.72447	1.026519	0.0003	3.602638	1.028273	0.0005
Boy's inattention at baseline	0.597664	0.099505	<.0001	0.625171	0.127732	<.0001	0.608514	0.127453	<.0001	0.61151	0.126506	<.0001	0.620846	0.127832	<.0001	0.630421	0.128903	<.0001
Boy's opposition at baseline	1.055148	0.142953	<.0001	0.273991	0.079745	0.0006	0.284294	0.080723	0.0004	0.27513	0.079544	0.0005	0.274467	0.079143	0.0005	0.270238	0.078988	0.0006
Boy's anxiety at baseline	-0.593143	0.083383	<.0001	0.128232	0.050675	0.0114	0.126959	0.05108	0.013	0.127242	0.050482	0.0117	0.126613	0.050761	0.0126	0.123109	0.051054	0.0159
Mother's age (years) at boy's birth	-0.088807	0.051883	0.0915	-0.116077	0.040293	0.0041	-0.109762	0.038739	0.0046	-0.110533	0.038908	0.0045	-0.108597	0.039758	0.0064	-0.095967	0.039593	0.0154
Father's age (years) at boy's birth	0.012328	0.042401	0.7722	0.057893	0.033669	0.0859	0.049377	0.033683	0.1433	0.052512	0.032341	0.1044	0.053213	0.033998	0.1181	0.042672	0.032866	0.1942
Mother's occupational prestige	-0.039662	0.01558	0.0122	-0.045998	0.011845	0.0001	-0.045202	0.011607	0.0001	-0.04415	0.012042	0.0003	-0.042958	0.012082	0.0004	-0.045121	0.011489	<.0001
Father's occupational prestige	-0.041919	0.015084	0.0063	-0.029255	0.010805	0.0072	-0.03098	0.010603	0.0036	-0.030542	0.010942	0.0058	-0.030897	0.010687	0.0041	-0.02677	0.010126	0.0082
Family intactness	-0.802497	0.380306	0.0353	-0.977357	0.37519	0.0092	-0.984606	0.376428	0.0091	-0.978043	0.366082	0.0076	-0.946444	0.377852	0.0124	-0.948658	0.36752	0.0099
Parent's depression	-0.617547	0.721847	0.4023	0.207588	0.418915	0.6214	-0.022046	0.408195	0.9571	-0.088081	0.37155	0.8126	-0.135354	0.449412	0.765	-0.163134	0.47129	0.7324
Parent's anxiety	1.84909	0.788719	0.0283	0.93595	0.587571	0.1196	0.923023	0.49068	0.0616	0.933846	0.475467	0.0505	1.016458	0.463231	0.0283	1.038569	0.527061	0.0535
Mother's use of cigarettes during pregnancy	0.307967	0.308001	0.3174	0.25389	0.254019	0.3176	0.25698	0.25702	0.3174	0.251648	0.251745	0.3175	0.254986	0.254999	0.3173	0.257427	0.257535	0.3175

[1] All estimates shown are multinomial logit coefficients derived from multivariate latent class regression

Table 3d. Tipping point sensitivity analysis to assess impact of violations of the missing at random assumption for parent's anxiety and its associated risk for high inattention symptom score trajectory based on mother ratings

	Original			Scale=0.87			Scale=0.90			Scale=1.10			Scale=1.14			Scale=1.15		
Parameter	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**	**Estimate**[1]	**Std Error**	**Pr > |t|**
High trajectory																		
Constant	1.015337	0.858858	0.2372	1.034688	0.895478	0.2485	1.076208	0.89239	0.2285	1.103666	0.901035	0.2216	1.206808	0.922321	0.1921	1.091371	0.88624	0.2186
Boy's inattention at baseline	0.331719	0.104834	0.0016	0.338412	0.103916	0.0011	0.330872	0.103294	0.0014	0.336838	0.103631	0.0012	0.333165	0.103877	0.0013	0.325668	0.104365	0.0018
Boy's opposition at baseline	0.112278	0.062084	0.0705	0.113461	0.06211	0.0678	0.108609	0.061914	0.0794	0.109482	0.062168	0.0783	0.108206	0.062041	0.0811	0.113649	0.061728	0.0656
Boy's anxiety at baseline	-0.003135	0.045553	0.9451	-0.002849	0.045452	0.95	-0.000683	0.045364	0.988	-0.002948	0.045346	0.9482	-0.002542	0.045437	0.9554	-0.004934	0.045168	0.913
Mother's age (years) at boy's birth	-0.064133	0.038629	0.099	-0.071886	0.035928	0.0455	-0.077046	0.036111	0.033	-0.065155	0.036062	0.0712	-0.070706	0.038467	0.0678	-0.067989	0.036486	0.0628
Father's age (years) at boy's birth	0.030801	0.033125	0.356	0.032655	0.029917	0.2752	0.038021	0.030341	0.2109	0.028705	0.029567	0.3318	0.032898	0.031118	0.2915	0.031414	0.030097	0.2969
Mother's occupational prestige	-0.017483	0.01164	0.1374	-0.019912	0.011279	0.0798	-0.018859	0.010701	0.0787	-0.019747	0.010813	0.0688	-0.021403	0.011086	0.055	-0.018723	0.010887	0.0866
Father's occupational prestige	-0.020023	0.010384	0.0551	-0.015366	0.010112	0.1298	-0.015715	0.010253	0.127	-0.017281	0.010733	0.1106	-0.01672	0.010023	0.0959	-0.016501	0.01046	0.117
Family intactness	-0.131372	0.291866	0.6528	-0.075557	0.285657	0.7914	-0.106768	0.289775	0.7126	-0.116677	0.289494	0.687	-0.133832	0.285106	0.6388	-0.147885	0.289691	0.6098
Parent's depression	0.553488	0.405225	0.1765	0.660121	0.398184	0.1012	0.605592	0.438632	0.1775	0.56023	0.355431	0.1155	0.635413	0.383394	0.1008	0.58532	0.399675	0.148
Parent's anxiety	1.061767	0.441637	0.0165	0.805261	0.51758	0.1277	0.93061	0.457924	0.0431	0.990653	0.474261	0.0417	1.005601	0.432687	0.021	0.891533	0.493441	0.0799
Mother's use of cigarettes during pregnancy	0.237585	0.237613	0.3174	0.239131	0.239205	0.3175	0.236423	0.23645	0.3174	0.238156	0.238187	0.3174	0.239189	0.239205	0.3173	0.236511	0.236557	0.3174

[1] All estimates shown are multinomial logit coefficients derived from multivariate latent class regression

Figure 1a. Directed acyclic graph of direct effects and mediation framework for hyperactivity symptom score trajectories, based on literature

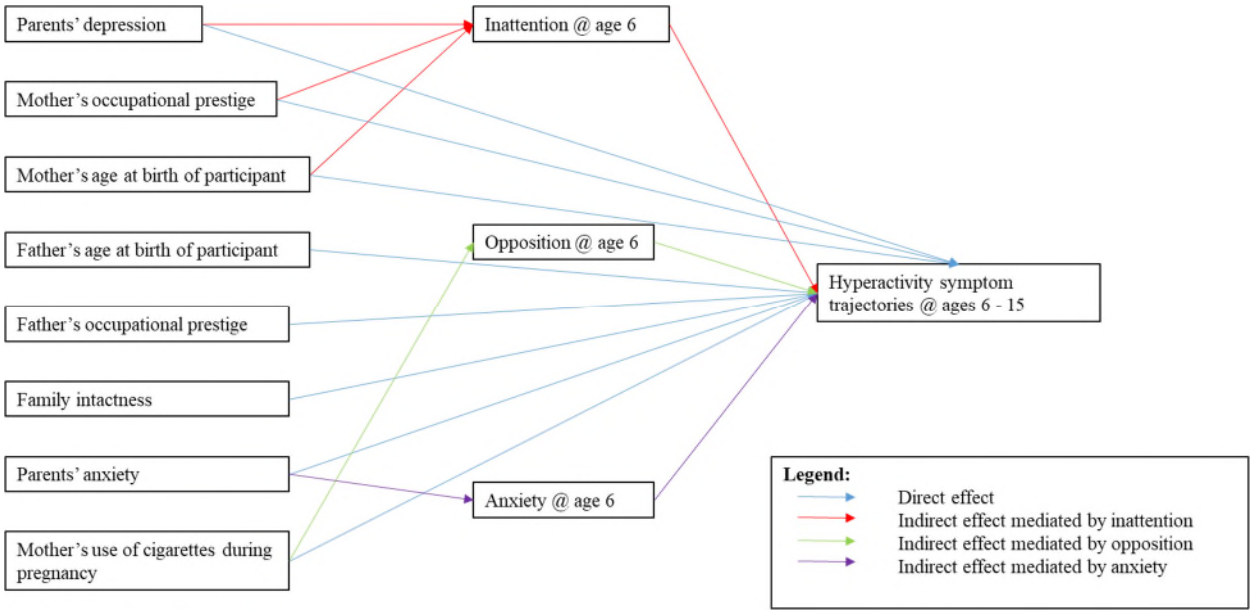


Figure 1b. Directed acyclic graph of direct effects and mediation framework for inattention symptom score trajectories, based on literature

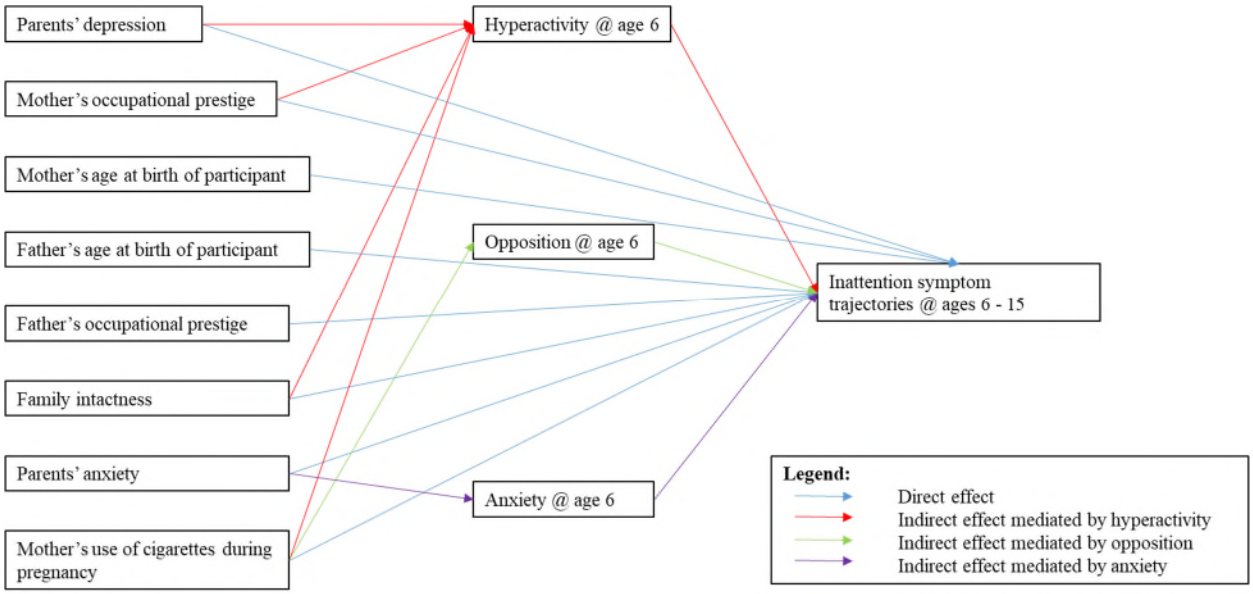


Figure 2a. Hyperactivity symptom score trajectories (teacher ratings) - Predicted trajectories and 95% CI

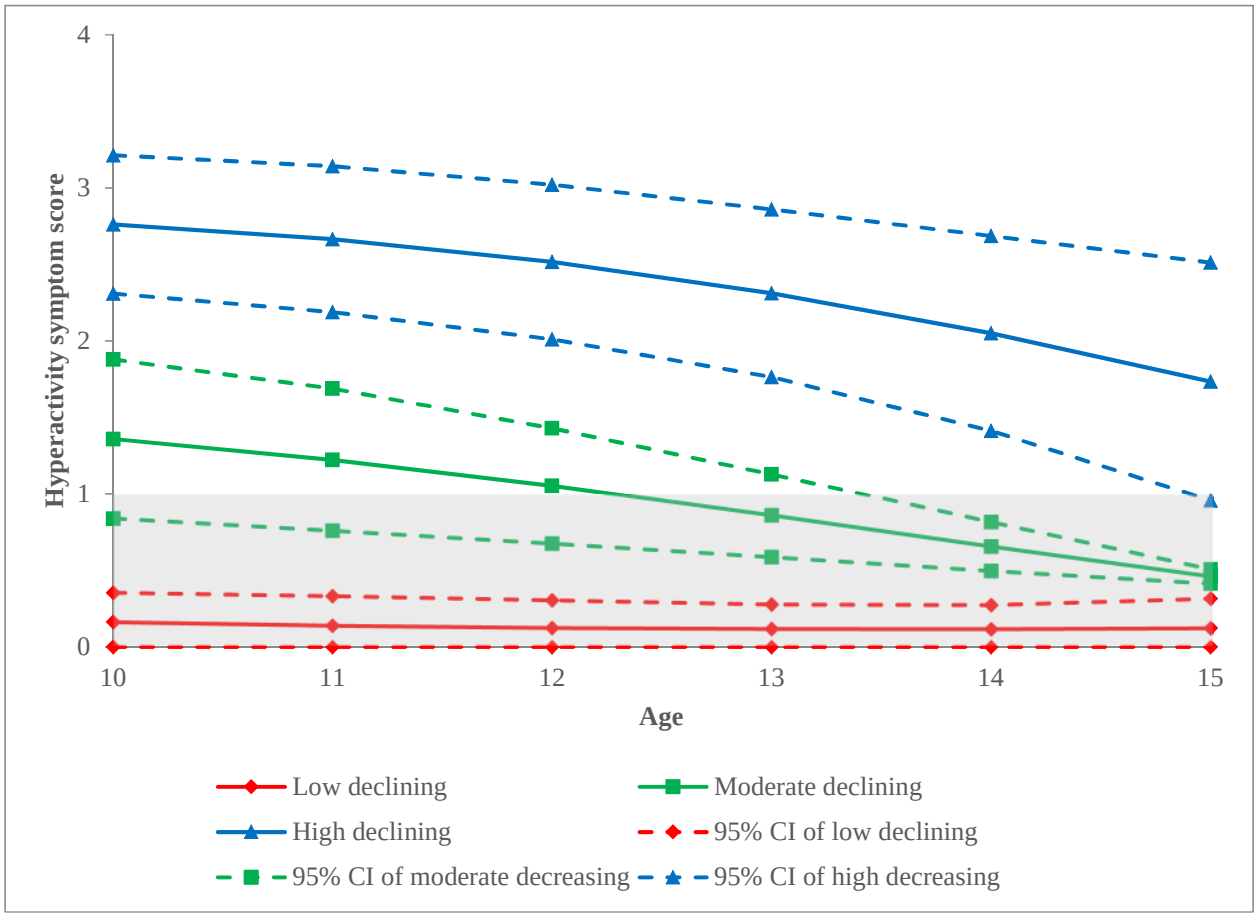


Figure 2b. Hyperactivity symptom score trajectories (mother ratings) - Predicted trajectories and 95% CI

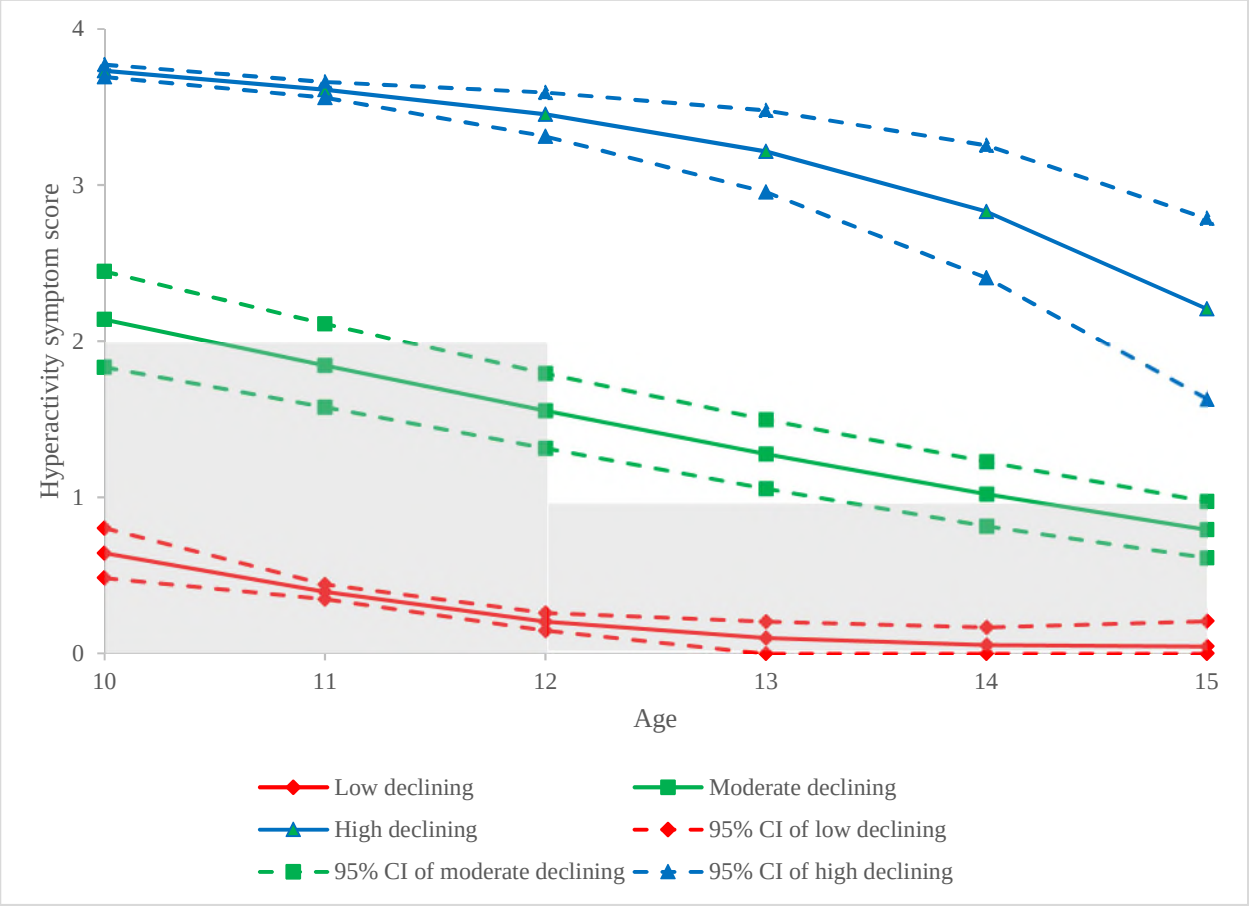


Figure 3a. Inattention symptom score trajectories (teacher ratings) - Predicted trajectories and 95% CI

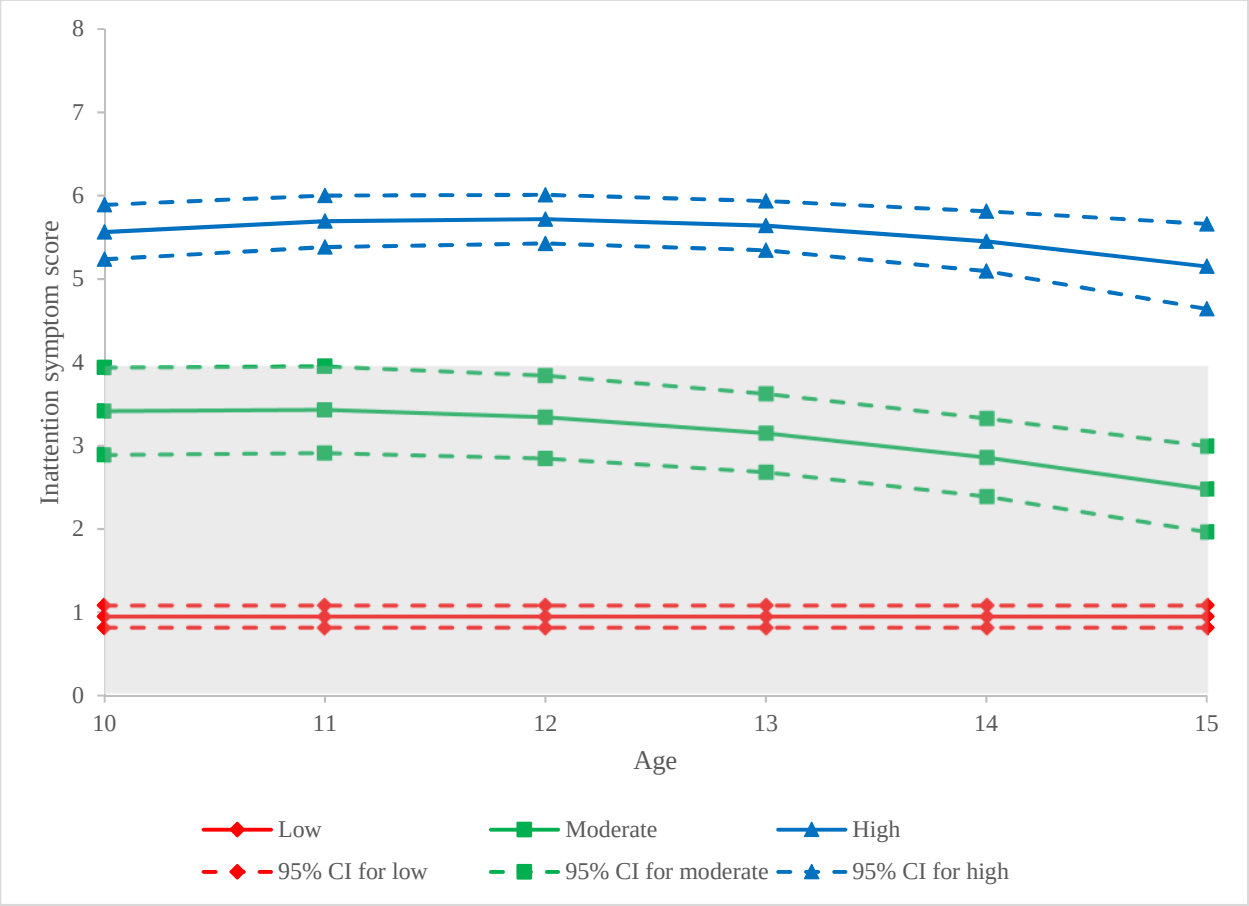
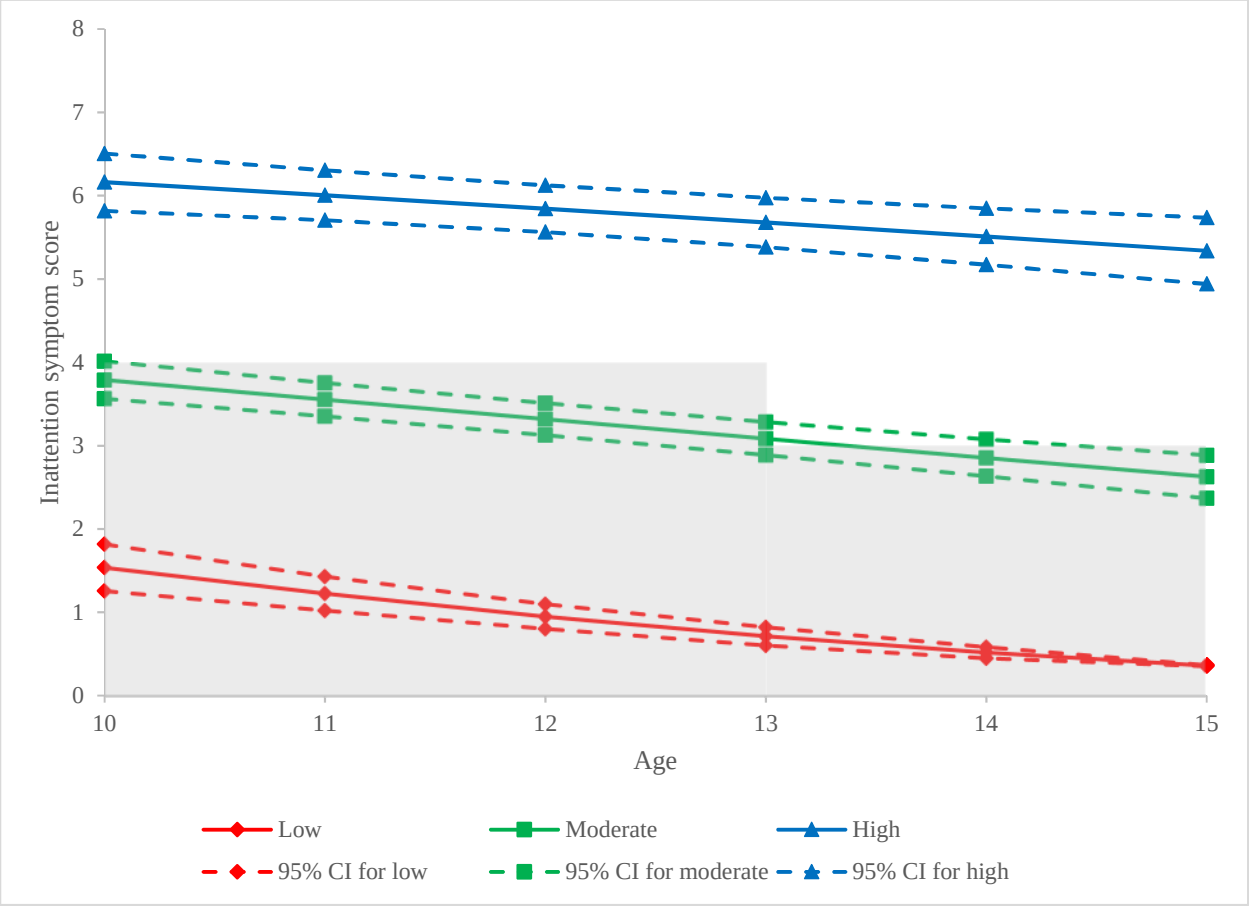


Figure 3b. Inattention symptom score trajectories (mother ratings) - Predicted trajectories and 95% CI



APPENDIX 3

Table 1. Confounding variables included in logistic regression models assessing associations between symptom score trajectories and cigarette smoking outcomes

	Hyperactivity symptom score trajectories		Inattention symptom score trajectories	
Cigarette smoking outcomes	**Teacher ratings**	**Mother ratings**	**Teacher ratings**	**Mother ratings**
Cigarette smoking frequency in late adolescence	▪ Participant's opposition at baseline ▪ Mother's smoking during pregnancy	▪ Participant's opposition at baseline	▪ Participant's hyperactivity at baseline ▪ Participant's opposition at baseline	▪ Participant's hyperactivity at baseline
Daily smoking in young adulthood	▪ Participant's inattention at baseline ▪ Participant's opposition at baseline ▪ Participant's anxiety at baseline ▪ Father's occupational prestige ▪ Family intactness	▪ Participant's inattention at baseline ▪ Participant's opposition at baseline	▪ Participant's hyperactivity at baseline ▪ Participant's opposition at baseline ▪ Participant's anxiety at baseline ▪ Father's occupational prestige ▪ Family intactness	▪ Participant's hyperactivity at baseline
Heavy smoking in young adulthood	▪ Participant's inattention at baseline ▪ Participant's opposition at baseline ▪ Father's occupational prestige ▪ Mother's smoking during pregnancy	▪ Participant's inattention at baseline ▪ Participant's opposition at baseline	▪ Participant's hyperactivity at baseline ▪ Participant's opposition at baseline ▪ Father's occupational prestige	▪ Participant's hyperactivity at baseline

Table 2a (Sensitivity analysis) Association between hyperactivity symptom score trajectories (teacher ratings) and cigarette smoking frequency in late adolescence

	Original			Scale=0.51			Scale=0.60			Scale=0.80			Scale=1.10			Scale=1.18		
Parameter	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**
Intercept 1	-0.096326	0.131175	0.4636	-0.41856	0.132061	0.0016	-0.32724	0.129811	0.0119	-0.17997	0.122726	0.1425	-0.05384	0.145419	0.7131	0.002702	0.13319	0.9839
Intercept 2	-0.965256	0.131212	<.0001	-1.02195	0.138913	<.0001	-0.99921	0.131689	<.0001	-1.02383	0.132727	<.0001	-0.88943	0.141782	<.0001	-0.79435	0.142811	<.0001
Moderate declining trajectory	0.473545	0.145709	0.0012	0.447774	0.147686	0.0024	0.44512	0.151802	0.0035	0.448551	0.14832	0.0026	0.439491	0.142617	0.0021	0.430275	0.146609	0.0035
High declining trajectory	0.677636	0.208969	0.0016	0.490854	0.198357	0.0134	0.551068	0.20702	0.0081	0.597113	0.200285	0.0031	0.741999	0.204757	0.0004	0.695535	0.195209	0.0004
Participant's opposition at baseline	0.021957	0.028672	0.4468	0.00512	0.025836	0.8429	0.008931	0.02759	0.7466	0.011293	0.027288	0.6796	0.029447	0.026891	0.2751	0.034371	0.025794	0.1831
Mother's use of cigarettes during pregnancy	-0.382016	0.13722	0.0069	-0.44932	0.190618	0.0355	-0.57248	0.158809	0.0012	-0.42891	0.163275	0.0161	-0.39536	0.16962	0.0331	-0.33559	0.159044	0.0468

Table 2b (Sensitivity analysis) Association between hyperactivity symptom score trajectories (teacher ratings) and daily cigarette smoking in young adulthood

	Original			Scale=0.76			Scale=0.80			Scale=0.90			Scale=1.09			Scale=1.10		
Parameter	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**
Intercept	0.129278	0.389275	0.7438	0.163887	0.343025	0.6354	0.220347	0.309221	0.4771	0.18476	0.36644	0.6186	0.298094	0.294722	0.3122	0.353203	0.318424	0.2702
Moderate declining trajectory	0.283179	0.194204	0.1564	0.319119	0.175998	0.0737	0.302968	0.188733	0.117	0.249557	0.198776	0.2214	0.225683	0.198287	0.2667	0.271212	0.178569	0.1348
High declining trajectory	0.492069	0.298687	0.1187	0.516094	0.251587	0.0459	0.632542	0.32924	0.0792	0.424127	0.310266	0.1933	0.496999	0.301457	0.1187	0.591881	0.270179	0.0366
Participant's inattention at baseline	0.119248	0.059516	0.0727	0.112628	0.040929	0.0073	0.137788	0.039587	0.0006	0.138837	0.053212	0.0207	0.109462	0.050414	0.0444	0.120811	0.051176	0.031
Participant's opposition at baseline	0.032844	0.037183	0.3838	0.01616	0.033145	0.6269	-0.00865	0.036484	0.8139	0.017377	0.036139	0.6334	0.031281	0.033844	0.3581	0.021529	0.031232	0.4909
Father's occupational prestige	-0.006095	0.006624	0.3672	-0.00838	0.006848	0.2346	-0.01031	0.006333	0.1124	-0.00827	0.006139	0.1855	-0.00928	0.006601	0.1732	-0.0099	0.006219	0.1201
Family intactness	-0.269422	0.206408	0.2083	-0.39461	0.220223	0.0952	-0.3544	0.167355	0.0367	-0.25454	0.181418	0.1685	-0.17616	0.195137	0.3757	-0.22174	0.189116	0.2503
Participant's anxiety at baseline	-0.091463	0.04576	0.0688	-0.11415	0.037602	0.0047	-0.10791	0.04098	0.0163	-0.1108	0.03894	0.0089	-0.08539	0.038875	0.0385	-0.09396	0.040183	0.03

Table 2c (Sensitivity analysis) Association between hyperactivity symptom score trajectories (teacher ratings) and heavy smoking in young adulthood

	Original			Scale=0.64			Scale=0.70			Scale=1.10			Scale=1.15			Scale=1.16		
Parameter	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**	**Estimate**	**Std Error**	**Pr > |t|**
intercept	-1.786324	0.514956	0.0053	-1.90864	0.442036	0.0001	-2.14721	0.424801	<.0001	-1.54575	0.577921	0.0275	-1.4165	0.331534	<.0001	-1.44251	0.40154	0.0013
Moderate declining trajectory	0.385115	0.290067	0.2056	0.353834	0.251863	0.1628	0.428532	0.245096	0.0829	0.351411	0.284654	0.2375	0.34254	0.206935	0.0996	0.352391	0.23495	0.1428
High declining trajectory	0.641824	0.346198	0.0819	0.614512	0.309067	0.0493	0.637001	0.365111	0.0955	0.585397	0.356612	0.1234	0.495205	0.254376	0.0523	0.517209	0.260253	0.0484
Participant's inattention at baseline	0.044027	0.03996	0.2726	0.024496	0.048556	0.6161	0.015232	0.045999	0.7415	0.034133	0.047657	0.4815	0.029527	0.056677	0.6126	0.01549	0.044248	0.7285
Participant's opposition at baseline	0.084426	0.036236	0.0213	0.086856	0.041046	0.0368	0.094487	0.04316	0.034	0.087899	0.039196	0.0302	0.101107	0.033473	0.0026	0.114259	0.038271	0.0044
Father's occupational prestige	-0.002897	0.009896	0.7752	-0.00688	0.008359	0.4137	-0.0005	0.008805	0.9556	-0.00644	0.008791	0.4746	-0.00787	0.006783	0.2476	-0.00755	0.006976	0.2824
Mother's use of cigarettes during pregnancy	-0.168526	0.241347	0.4979	-0.35681	0.311449	0.2807	-0.26316	0.292052	0.389	-0.17172	0.220584	0.4479	-0.28762	0.323577	0.4045	-0.23253	0.303656	0.4677

Table 3a (Sensitivity analysis) Association between inattention symptom score trajectories (teacher ratings) and cigarette smoking frequency in late adolescence

	Original			Scale=0.50			Scale=0.60			Scale=0.80			Scale=1.10			Scale=1.20		
Parameter	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|
Intercept 1	-0.299728	0.157982	0.0597	-0.57141	0.151704	0.0002	-0.53191	0.153866	0.0006	-0.42884	0.155219	0.006	-0.27975	0.159118	0.0812	-0.22079	0.149943	0.1414
Intercept 2	-1.167739	0.169379	<.0001	-1.16195	0.155551	<.0001	-1.21492	0.156324	<.0001	-1.2547	0.158667	<.0001	-1.12923	0.163398	<.0001	-1.00359	0.163483	<.0001
Moderate declining trajectory	0.29183	0.187292	0.1219	0.201465	0.177667	0.2568	0.22665	0.177495	0.2017	0.321473	0.180142	0.0749	0.347228	0.178677	0.0528	0.352556	0.172702	0.0414
High declining trajectory	0.626925	0.196171	0.0018	0.433435	0.187623	0.0209	0.498998	0.189279	0.0085	0.603866	0.197695	0.0027	0.699995	0.187529	0.0002	0.680534	0.19076	0.0004
Participant's hyperactivity at baseline	0.013572	0.058755	0.8179	-0.01094	0.05473	0.8415	-0.01671	0.053687	0.7556	0.005776	0.054851	0.9162	0.021025	0.054207	0.6983	0.028655	0.058749	0.6269
Participant's opposition at baseline	0.03746	0.033105	0.262	0.022893	0.029861	0.4433	0.032119	0.029993	0.2843	0.021766	0.032363	0.5028	0.036104	0.031792	0.2584	0.023744	0.032153	0.462

Table 3b (Sensitivity analysis) Association between inattention symptom score trajectories (teacher ratings) and daily cigarette smoking in young adulthood

	Original			Scale=0.37			Scale=0.38			Scale=1.10			Scale=1.20			Scale=1.67		
Parameter	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|
Intercept	-0.013811	0.437826	0.9752	-0.7526	0.359259	0.0378	-0.75791	0.359498	0.0367	0.120068	0.381759	0.7552	0.106816	0.426842	0.8053	0.242554	0.360769	0.5042
Moderate declining trajectory	0.442259	0.237903	0.0744	0.246321	0.2028	0.2245	0.254376	0.202018	0.208	0.407473	0.193225	0.0356	0.455211	0.205092	0.0287	0.418071	0.245368	0.1043
High declining trajectory	0.981358	0.265851	0.0014	0.414222	0.213033	0.0518	0.42485	0.213232	0.0463	1.012174	0.259889	0.0007	1.075864	0.250232	0.0002	1.088281	0.223691	<.0001
Participant's hyperactivity at baseline	0.070729	0.0799	0.3882	0.02945	0.064176	0.6468	0.029766	0.065497	0.6503	0.06663	0.073238	0.3705	0.086676	0.078552	0.2831	0.059736	0.06403	0.3522
Participant's opposition at baseline	0.037855	0.044183	0.402	0.029499	0.035091	0.401	0.030635	0.035771	0.3926	0.044923	0.047464	0.3589	0.025421	0.046616	0.5929	0.038256	0.03659	0.2973
Father's occupational prestige	-0.007712	0.007189	0.2983	-0.00473	0.006023	0.4338	-0.00476	0.00606	0.4338	-0.00769	0.005916	0.1983	-0.00906	0.008316	0.3001	-0.00824	0.006276	0.197
Family intactness	-0.22299	0.197516	0.2705	-0.05811	0.162101	0.7201	-0.05634	0.160876	0.7263	-0.27144	0.201681	0.1917	-0.19975	0.18357	0.2826	-0.27081	0.191376	0.1659
Participant's anxiety at baseline	-0.0776	0.032657	0.0247	-0.0608	0.027989	0.03	-0.05918	0.028775	0.0404	-0.0745	0.034097	0.04	-0.06825	0.030761	0.0316	-0.05096	0.036406	0.1802

Table 3c (Sensitivity analysis) Association between inattention symptom score trajectories (teacher ratings) and heavy smoking in young adulthood

	Original			Scale=0.75			Scale=0.85			Scale=0.91			Scale=1.20			Scale=1.30		
Parameter	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|	Estimate	Std Error	Pr > |t|
intercept	-2.040476	0.426867	<.0001	-2.19619	0.393001	<.0001	-1.95931	0.487883	0.0005	-1.96936	0.455991	0.0001	-1.91828	0.422695	<.0001	-1.6765	0.458748	0.0017
Moderate declining trajectory	0.421546	0.273598	0.1246	0.375959	0.276173	0.1735	0.437826	0.296825	0.1428	0.344818	0.308008	0.2681	0.363075	0.263473	0.17	0.387929	0.253211	0.1263
High declining trajectory	0.668095	0.288307	0.0218	0.583682	0.300333	0.0533	0.603918	0.304721	0.0496	0.655181	0.282507	0.0209	0.721086	0.32542	0.0367	0.748636	0.257916	0.0039
Participant's inattention at baseline	0.043791	0.07487	0.56	0.046225	0.080551	0.5678	0.046759	0.083338	0.5776	0.023902	0.088154	0.7884	0.049244	0.076331	0.522	-0.00795	0.10908	0.9434
Participant's opposition at baseline	0.108586	0.041849	0.0123	0.102156	0.043267	0.0213	0.089205	0.046104	0.0619	0.103052	0.050262	0.0553	0.100815	0.040872	0.0173	0.103276	0.058336	0.1089
Father's occupational prestige	-0.002176	0.007824	0.7825	-0.00167	0.006789	0.8054	-0.00657	0.010342	0.5372	-0.00426	0.007904	0.5926	-0.00086	0.007126	0.9046	-0.00501	0.009032	0.5881